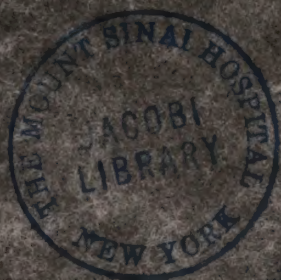


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JOURNAL OF THE MOUNT SINAI HOSPITAL NEW YORK

DIPHTHERIA IMMUNIZATION AND THE CONTROL OF DIPHTHERIA AS OBTAINED WITH ANATOXIN

RESULTS; PROGRESS¹

G. RAMON

Quelques années avant sa mort, Emile Roux qui, en 1887, avait découvert la toxine diphtérique, recevait à l'Institut Pasteur Bela Schick. "Vous avez," lui dit-il, "fait accomplir un grand progrès à l'étude de l'immunité antidiphtérique. La réaction de Schick en fournissant un moyen très commode de mesurer le degré de cette immunité a rendu possible la démonstration rapide de l'efficacité de la vaccination contre la diphtérie. . . ."

Dans une publication récente,² je m'exprimais moi-même ainsi: "C'est en 1913 que Behring en Allemagne fit connaître ses premières tentatives d'immunisation active, chez l'homme, à l'aide des mélanges de toxine et de sérum antidiphtérique. Vers le même temps et indépendamment de lui, William H. Park procédait à des essais de vaccination chez les enfants de New York, en utilisant, lui aussi, des mélanges de toxine et d'antitoxine. Favorisés par la découverte que Bela Schick venait de faire (1913) et qui permettait par une simple épreuve intradermique (avec une dilution très forte de toxine diphtérique) de se rendre compte de l'état d'immunité des individus, les essais de W. H. Park et de ses collaborateurs, aux Etats-Unis, prirent durant plusieurs années une certaine ampleur: ils eurent le grand mérite de montrer la voie à suivre pour l'organisation de la prophylaxie de la diphtérie au moyen d'une vaccination spécifique; ils fournirent l'occasion de réunir une documentation importante sur l'épidémiologie de la diphtérie et de recueillir, grâce à l'épreuve de Schick, des renseignements des plus intéressants quant à la fréquence de l'immunité antidiphtérique naturellement acquise."

Au seuil du présent article consacré à la vaccination antidiphtérique au moyen de l'anatoxine j'ai tenu à rendre hommage aux pionniers de la lutte contre la diphtérie et tout spécialement à Bela Schick.

¹ Dedicated to our colleague and friend Bela Schick on the occasion of the twenty-fifth anniversary of the discovery of the "Schick test."

² G. Ramon. Annales de Médecine. T. 42: No. 3, p. 314, 1937.

DIPHTHERIA ANATOXIN AND ITS PROPERTIES

After having described, in 1922,³ the phenomenon of flocculation occurring in mixtures of filtered diphtheria bouillon and diphtheria serum and having employed it as a method of determining the presence and quantity of specific toxin and antitoxin *in vitro*, we showed beyond any possibility of question⁴ that the diphtheria toxin may, under certain conditions, become transformed into a harmless product, which retains both the flocculating property and the immunizing power of the toxin and which also possesses new properties.⁵ Such is the case, for example, with the product obtained by subjecting diphtheric bouillon to the simultaneous action of heat and of a small quantity of formalin. We designated this new product by the term *anatoxin*.

Anatoxin has two essential properties, namely, harmlessness and intrinsic antigenic value.

Harmlessness is the character which distinctly differentiates anatoxin from the toxin from which it is produced and which justifies the term which has been applied to it. For any anatoxin prepared and checked according to the principles which we have established, its harmlessness should be not only relative, but absolute.

We are at present able to report that we have produced, tested and distributed throughout the world, through the invaluable coöperation of our collaborators, more than twenty thousand liters of diphtheria anatoxin, capable of providing at least several millions of injections, and considerably more than ten millions, were the entire quantity fully utilized. Thus far, no incident, complication or accident has occurred which can be responsibly assigned to any trace, however slight, of toxicity remaining in the anatoxin which we ourselves prepare. *This fact proves both the positive harmlessness of anatoxin and the efficacy of the precautions observed to insure its harmlessness.*

Anatoxin is not characterized by harmlessness alone.

Since the memorable work by Roux and Yersin on the diphtheria toxin, accomplished half a century ago, and which has served as a genuine and necessary introduction to antitoxic serotherapy, many methods of attenuating or destroying the harmfulness of bacterial poisons have been made known. Many physical, chemical and biological agents have been employed, formerly and latterly, by experimenters who were far more interested in abolishing injurious characters than they were in preserving certain other properties of toxins which were more important. Anatoxin

³ G. Ramon. C. R. de la Soc. de Biol., 86: 661-711-713, 1922. Ann. Inst. Pasteur, 37: 1001, 1923.

⁴ G. Ramon. The flocculating and toxic capacity of diphtheric toxin. C. R. de la Soc. de Biol., 89: 2, 1923.

⁵ G. Ramon. The flocculating capacity and immunizing properties of a diphtheric toxin rendered anatoxic (anatoxin). C. R. de l'Acad. des Sciences, 177: 1338, 1923.

would represent merely relative progress in the preparation of antigens and would contribute nothing new to the practice of antitoxic immunization were it only a diphtheria bouillon possessing toxicity more or less altered by formic aldehyde. An "anatoxin" is not obtainable merely by adding a little formalin to a diphtheric toxin, although such was supposed to be the case at one time and such is the practice employed by certain investigators.

Löwenstein allowed formaldehyde to act upon the diphtheria poison, but failed to destroy its harmfulness completely and was unable to make use of his product for the immunization of animals, to say nothing of immunizing human individuals; and while Glenny and his collaborators were more fortunate, they succeeded only through new information supplied in this field through the development of the flocculation reaction by us and by means of deductions derived from it. As Glenny stated, as early as 1924,⁶ *"the flocculation test has given a great impetus to the study of modified toxins."* As a matter of fact, as we have established, *anatoxin is not merely a toxin rendered harmless by the combined action of formin and heat, or by any other means, but its principle includes not only the element of harmlessness, but also that of intrinsic antigenic value, as indicated by the flocculation reaction.*

Practically, the intrinsic antigenic value of an anatoxin is expressed in terms of antitoxic units. It corresponds to the number of antitoxic units capable of producing initial flocculation in one cubic centimeter of anatoxin. In order to facilitate international comparisons and exchanges, the standardization committee of the League of Nations has defined a standard flocculation serum which serves as a common unit of measurement. The numerous experiments undertaken with animals and the many tests made in man by means of vaccination have proved that *the intrinsic antigenic value determined by flocculation constitutes the index, as exactly as may possibly be obtained, of the ability to produce immunity which is inherent in the constitution of the anatoxin.*

Anatoxin is characterized by still other properties, including *stability, thermo resistance, and irreversibility.*

From his prolonged and excellent studies, continued for several years, S. Schmidt, of Copenhagen,⁷ concludes that *"we consider, with Ramon, that anatoxin is a new modification of a toxin."*⁸

In point of fact, an entire group of properties, including harmlessness, intrinsic antigenic value corresponding to the power of inducing an abundant formation of antitoxin within the human or animal organism, stability, special capacity for resisting heat, and irreversibility, differentiate anatoxin from all

⁶ Glenny. Journ. of Path. and Bact., 27, 270, 1924.

⁷ S. Schmidt. The action of certain organic compounds upon diphtheria toxin. Acta Pathologica et Microbiologica Scandinavica. Supplement 12, 1932.

⁸ S. Schmidt. Ann. Inst. Pasteur, 45: 337, 1930.

other antigens thus far known, render it a new substance and impart to it an individual existence, justifying the term which has been applied to it and permanently insured by experimentation and practical application which have come at present to have an extension of the most general kind.

On account of its safety, its immunizing activity and its other qualities, anatoxin is especially adapted and designed for the vaccination of man against diphtheria. We therefore proposed it for this object as soon as it was discovered.⁹



Dr. Bela Schick and Dr. G. Ramon in the park of the Pasteur Institute at Garches, Paris

By the close of 1933, tests of diphtheria vaccination by means of anatoxin were being undertaken. The many preliminary experiments which we made with animals, and which supplied invaluable information concerning the conditions most favorable for inducing immunization, such as dosage of anatoxin, intervals elapsing between injections and similar practical points, enabled us promptly to establish the technique of vaccination as applied to man. In this way we finally fixed the appropriate interval to elapse between the vaccinal injections at three weeks. This technique came finally to be generally adopted. It is based upon the stimulating effect produced by a new injection of anatoxin, separated from a preceding injection by a certain period of time.

⁹ G. Ramon. C. R. de l'Acad. des Sciences, 177: 1328, 1923.

A short time after anatoxin was discovered A. Zingher, collaborating in New York with William Park in his campaigns of prophylaxis against diphtheria, in which mixtures of toxin and antitoxin were employed, was therefore especially qualified to express an opinion concerning diphtheria vaccination. From personal tests of anatoxin supplied to him by us, he concluded that "*diphtheria anatoxin is an ideal preparation for active immunization against diphtheria.*"¹⁰

In a very recent article, published in November, 1937,¹¹ William Park writes, "*In 1924 Zingher and I¹² accepted the superiority of Ramon's anatoxin—or, as it is called in this country, the formol toxoid—as compared with toxin-antitoxin. We summed up this superiority by stating that toxoid is a) more stable, b) easier to prepare, c) not dangerous if accidentally frozen, d) more effective and e) nonsensitizing.*"

Dating from 1924, diphtheria anatoxin began to be more and more generally employed in France for active immunization and the prophylaxis of diphtheria. The method gradually extended to other countries and during the last few years its use has become world-wide.¹³ Up to the present time, it has been applied to tens of millions of persons.

The conference of experts held under the auspices of the Committee on Hygiene of the League of Nations and meeting in London, in 1931, with Madsen, also President of the League committee, as chairman, *recognized the harmlessness and efficacy of vaccination by means of diphtheria anatoxin and recommended this method.*

DIPHTHERIA IMMUNIZATION AS OBTAINED WITH ANATOXIN—ITS RESULTS AS JUDGED BY THE SCHICK TEST

When the method here discussed was first applied, and until a few years ago, the technique employed was, in general, that which we had established, three subcutaneous injections of anatoxin, respectively of 0.5, 1, and 1.5 cc., being given, three weeks apart. The anatoxin employed in France during the earlier years, and until 1929, contained 10 antigenic units (Lf.) per cubic centimeter. Onward from 1930, as we shall see, the value of the anatoxin was progressively increased, at present consisting of at least 30 units per cubic centimeter.

A. Value of the immunity conferred by anatoxin

The first trials of immunization were regularly checked and controlled by the *Schick test*,¹⁴ the following points being thus established.

¹⁰ A. Zingher. Proc. Soc. for exp. biol. and med., 462, 1935.

¹¹ William Hallock Park. Journ. of the A. M. A., CIX, No. 21, 1681, 1937.

¹² W. H. Park and Abraham Zingher. Am. Journ. of Diseases of Children, 28: 464, 1924.

¹³ Detailed account of its distribution is beyond the scope of the present paper. For such an account, see our general review, Ann. de Méd., 42: 314, 1937.

¹⁴ For fuller details, see Ann. Inst. Pasteur, 42: 1928.

After the first injection, of 0.5 cc., or 10 units, of anatoxin, the Schick test is negative in 40 per cent of the individuals whose original reaction was positive.

After two injections, of 0.5 and 1 cc., respectively, and given three weeks apart, the negative reactions obtained number 80 per cent to 90 per cent.

After three injections, of 0.5, 1, and 1.5 cc., respectively, the Schick reactions becoming negative generally reach a proportion of 95 per cent and sometimes exceed it.

These results were very generally confirmed in other countries. We present here the results obtained in the United States by a comparative use of anatoxin and mixtures of toxin and antitoxin (T. A.). In Chicago, G. F. and G. H. Dick vaccinated adult nurses, of whom some received *five injections* of toxin-antitoxin (type O, I L+, Park), the others receiving *three injections* of anatoxin, supplied by ourselves. The results are indicated below.¹⁵

Number of individuals receiving 5 doses T. A., type O, I L+, Park.....	100
Schick test checks negative.....	82
Schick test checks positive.....	18
Number of individuals receiving 3 injections anatoxin.....	100
Schick test checks negative.....	94
Schick test checks positive.....	6

A. Schwartz and F. R. Janney vaccinated school children at Milwaukee, Wisconsin, their results being tabulated as follows:¹⁶

	<i>per cent</i>
Schick test checks negative after vaccination with 3 doses T. A. mixture.....	75
Schick test checks negative, after vaccination with 3 doses anatoxin ..	98
Schick test checks negative, after vaccination with a toxin attenuated by sodium ricinoleate (Larson).....	60

Weinfeld and Cooperstock, of Ann Arbor, Michigan,¹⁷ and S. Thompson, of Gary (Indiana), Claire E. Healey,¹⁸ show practically equivalent results.

W. T. Harrison, of the United States Public Health Service, at Washington, stated, in 1930¹⁹ that, of 475 children receiving injections of anatoxin, 95 per cent acquired immunity sufficient to present Schick-negative reactions, while of 355 children vaccinated with injections of a toxin-antitoxin mixture (type O, I L+), only 64 per cent gave negative Schick tests. These results are of particular importance, for they were obtained with

¹⁵ G. F. and G. H. Dick. Journ. of the A. M. A., XCII, 1901, 1929.

¹⁶ A. Schwartz and F. R. Janney. Am. Journ. Dis. of Chil., XXXIX, 504, 1930. See also Journ. of the A. M. A., XCIV, 1708, 1930.

¹⁷ Weinfeld and Cooperstock. Journ. of the A. M. A., XXXVIII, 35, 1929.

¹⁸ Claire E. Healey, Journ. of the A. M. A., T 105: 1935, p. 1182.

¹⁹ W. T. Harrison. Public Health Reports, XLV, No. 33, 1883, 1930.

samples of anatoxin and a toxin-antitoxin mixture supplied by various manufacturers for general and ordinary use and tested by the National Hygienic Laboratory, at Washington.

The comparative results thus rendered applicable by the Schick test have clearly confirmed the high superiority of the diphtheria immunization produced by the use of anatoxin. We desire to direct attention to the fact that, while it is relatively easy to render the Schick test negative in 70 per cent to 80 per cent of the vaccinated individuals, it is vastly more difficult to attain a higher result, like 94 per cent, or 98 per cent, results which are obtainable regularly and readily by vaccination correctly applied by the method employing anatoxin.

In the course of our own checking and control, we have examined, on various occasions, the relation existing between the Schick findings in individuals vaccinated with anatoxin and the quantity of specific antitoxin present in the serums of the same individuals. The antitoxin was determined by a method applying to guinea pigs, derived directly from the fundamental technique of Ehrlich, which is the most precise for application to this special field.

As an example, we offer an account of one of our tests, performed with the collaboration of Robert Debré, M. and G. Mozer and G. Pichot.²⁰ In this test, 105 children at the Seaside Hospital at Berck, previously vaccinated with anatoxin, were examined. Determinations of the antitoxic activity of the serums of these 105 children gave the results appearing below.

	<i>per cent</i>
Antitoxic activity of more than 1 unit, in 43	40.9
Antitoxic activity of more than 1/10 unit, in 52	49.2
Antitoxic activity of more than 1/30 unit, in 6	5.7
Antitoxic activity of less than 1/30 unit, in 4	3.8

The antitoxin thus exceeded 1/30 unit in 96 per cent of the members of this group.

The Schick test was applied to these 105 children at the same time. It was negative in 101, or 96 per cent, and was positive in 4, who were the same individuals whose antitoxic activity following vaccination was below 1/30 unit.

Contrary to certain cases which we do not consider valid, this investigation proves that a Schick-negative reaction refers to a serum containing antitoxin in excess of 1/30 unit and confirms the great value of the Schick test.

B. Duration of the immunity conferred by anatoxin

The duration of the immunity conferred by anatoxin is a point of importance. It has been examined from time to time during the development of anatoxic immunization.

²⁰ See Ann. Inst. Pasteur, 45: 326, 1930.

With the collaboration of R. Debré, M. and G. Mozer, and G. Pichot,²¹ we considered this question in 1929, examining children previously vaccinated with 3 doses of anatoxin, respectively of 0.5, 1, and 1.5 cc., given three weeks apart. The Schick reaction was negative in 97.5 per cent of these children, four years after the vaccination. It was negative in 100 per cent of the children vaccinated three years previously, negative in 94 per cent of those vaccinated two years previously, and negative in 92 per cent of those vaccinated one year before. These results show most clearly that, while the immunity conferred by anatoxin may slightly diminish during the first year, it tends to increase again later on, apparently through the influence of *natural immunization*.²²

Our colleague G. Loiseau has made similar observations, which, as a whole, confirm our results. On examining children seven years after vaccination, the Schick reactions were negative in 95.7 per cent of them. In another group examined by G. Loiseau, the Schick tests were negative in 100 per cent of its members, eight years after vaccination.

Julius Blum, of New York, has recently stated as follows: "In 103 children who received two injections of unmodified fluid toxoid of 1 cc. each two weeks apart, there was no loss in immunity in seventeen cases at nine months, in 7.5 per cent in sixty-six cases at from one to two years, and no loss in twenty cases at from two to three years."²³

The immunity produced by correctly applied anatoxic vaccination thus appears to persist, soundly and durably, for many years.

ANATOXIC VACCINATION AND ITS INFLUENCE UPON THE MORBIDITY AND MORTALITY OF DIPHTHERIA

Aside from the immunity conferred by anatoxin and which may be verified by the Schick test, information concerning the actual practical value of anatoxic vaccination is available from epidemiological sources. We present examples taken from countries in which the method has been largely employed and which show its influence upon diphtheria morbidity and mortality.

As we have indicated in introducing this article, anatoxin has replaced mixtures of toxin and antitoxin in the United States, mainly through the efforts of William Park of New York who, after having been a principal initiator of the T. A. vaccines, became an ardent advocate of anatoxin. The results shown by the statistics published in New York are entirely decisive. The present mortality due to diphtheria is at present 1.2 per 100,000 inhabitants. In 1916, it was 22 per 100,000, and in 1929 it was

²¹ G. Ramon, R. Debre, M. and G. Mozer and G. Pichot. Ann. Inst. Pasteur, 45: 326, 1930. Am. Journ. of Diseases of Children, 61: 1931, pp. 1-7.

²² See G. Ramon. Rev. d'Immunol., 2: 395, 1936.

²³ Cited by William Park. See also Julius Blum, abstract of discussion, Journ. of the A. M. A., CIX, No. 21, 1684, 1937.

6.7 per 100,000. Never have diphtheric morbidity and mortality been as low in the United States as they now are. This result is due to active propaganda and systematic campaigns conducted in favor of diphtheria vaccination, which should be imitated elsewhere.

Scarcely had the early tests of immunization been realized in France, in 1923 and 1924, when prophylaxis against diphtheria was begun in *Canada*, through the use of anatoxin, prepared and employed according to our method. Through the energetic efforts of FitzGerald, who collaborated with Defries, Fraser, Moloney and others, this new attempt at prophylaxis became practiced rapidly, and on a large scale. Of a population numbering ten million inhabitants, more than one and a half million have been vaccinated, thus far. A general survey of the statistics shows that nine-tenths of the diphtheria morbidity have been abolished by vaccination. Still more demonstrative are the results obtained in some of the larger Canadian cities, such as Toronto and Hamilton. In the latter city, whose inhabitants number 150,000, more than 85 per cent of the children were vaccinated against diphtheria between the years 1924 and 1932. In 1931, only a few cases of diphtheria occurred, with no mortality.

As recently indicated by J. C. FitzGerald, D. T. Fraser and N. E. McKinnon, at the Congress on Microbiology, London, 1936, the widely extended use of diphtheria anatoxin according to our method, which employs three injections, has reduced both the morbidity and the mortality of diphtheria. Its efficacy in the prophylaxis of diphtheria has now become fully established.

During recent years, several antidiphtheria campaigns have been undertaken in *Switzerland*. In 1932, anatoxic vaccination was made *obligatory* for school children in the canton of Geneva. Audeoud states that popular excitement there subsided, after a few protests. In February, 1936, the General Council confirmed the principle of obligatory vaccination decreed by the canton of Geneva and the children of this canton are now vaccinated legally. According to Rillet, 64 cases of diphtheria occurred at Geneva, in 1931, where the cases numbered 25 in 1932. According to Reh, only a few cases of diphtheria occurred in 1933, in vaccinated individuals, none proving fatal. During the past three years, diphtheria morbidity has diminished in the canton of Geneva, on account of the obligatory practice of vaccination there. Some of the other Swiss cantons are preparing to follow this example. Audeoud has recently stated that no fatal cases of diphtheria occurred among vaccinated children, during the period between 1929 and 1936.²⁴

In the *Union of Soviet Socialist Republics* (U. S. S. R.), antidiphtheric vaccination as applied by our method was widely adopted, as soon as it became known. Excellent results were obtained by Barikine, Netchadi-

²⁴ H. Audeoud. *Revue Méd. Suisse Romande*, 19: 294, 1937.

menko, Isabolinski and others. Through the efforts of Zdrodowski, particularly remarkable results occurred at Baku, Leningrad and Moscow.²⁵ Hundreds of thousands of children have been vaccinated in the Union of Soviet Socialist Republics. In Leningrad alone, 357,000 children were vaccinated between the years 1932 and 1934. Korsakoff points out that the diphtheric morbidity at Leningrad among vaccinated children is but one-fourteenth of that occurring with the unvaccinated.

For the sake of reference, we mention some of the resolutions adopted by the anti-epidemic conference of the U. S. S. R., held in June, 1935, after considering reports presented by Zdrodowski and Zaharow, as follows: "In view of the regular decline in diphtheria morbidity and mortality in children who are vaccinated, as compared with these factors in unvaccinated children, the conference considers that the unquestionable harmlessness and efficacy of preventive vaccination against diphtheria are fully proved. The conference therefore considers opportune and necessary publication by the Government of a special law concerning preventive vaccination against diphtheria, which should provide for the regulation of the following points: (1) Preventive vaccination is applied as a regular and obligatory prophylactic measure to children aged six months to twelve years. (2) Preventive vaccination is employed in conformity with a single regulation, which shall be obligatory for all the component republics of the Union and promulgated by the Sanitary Inspection Service of the Union of Soviet Socialist Republics.

The conference also considers that the single regulation governing the active immunization against diphtheria should be based upon the following rules: (a) Children aged 6 months to 12 years must be vaccinated. (b) The diphtheria anatoxin of Ramon, containing at least 20 antigenic units per cubic centimeter, is the only preparation accepted for this purpose. Vaccination shall include two injections, respectively of 1 cc. and 2 cc., given three weeks apart. Revaccination by the so-called "recall" or "repeat" injection shall be applied six to twelve months after the regular vaccination." Briefly, this method is the one which we have always recommended and which is thus officially adopted in the Union of Soviet Socialist Republics.

We likewise present a few details referring to the epidemiological results accomplished in *France* after the application of anatoxic vaccination. Effects of this method have been shown by progressive reduction of the urban diphtheria morbidity and mortality in cities and regions where this form of vaccination has been systematically practiced.

At *Paris*, the diphtheria mortality has been regularly declining since 1928. In 1936, for example, deaths from diphtheria were 211 less than those for the year 1928, in which year the total diphtheric mortality was

²⁵ For an excellent biological and immunological study by Zdrodowski and Halapine, see the *Revue d'Immunologie*, 2: 221, 1936.

318, the figure for 1936 being 107. The fatal cases numbered only 64 during the first nine months of 1937. The figures for 1936 and 1937 are the lowest known since statistical records were established. The diphtheria mortality per 100,000 inhabitants has declined from 11.1, in 1928, to 3.7, in 1936.

How is it possible not to assign the diminution at present observed in the diphtheria mortality at Paris to the anatoxic vaccination which has been increasingly employed there during the last few years? In order to explain at least a part, if not all, of this diminution, the latter might perhaps be attributed to the decline or cessation of an epidemic condition. Yet has not diphtheria continued to occur at Paris, with the same frequency present in other cities among the child population not receiving vaccination?

Chalut, Director of the Hygienic Services in the French region of the Rhône has recently made the following observations at *Lyons*: Of 987 children, 402 were vaccinated; children affected with diphtheria numbered 71 and the fatal cases numbered 6. With vaccinated individuals, the morbidity was 1.5 per cent, while with the unvaccinated it was 11 per cent. Among cases of diphtheria where vaccination had been previously applied, there were no deaths, while the mortality was 9.5 per cent in cases where vaccination had not been utilized. However, instead of offering general statistical tabulations, which are accepted by some and whose real value is questioned by others, we present concrete examples showing what may be accomplished in the prophylaxis of diphtheria by the correct and systematic application of anatoxic vaccination to population groups of more or less extent and importance.

First, we offer the results obtained by L. Martin, G. Loiseau and A. Laffaille,²⁶ at the *primary departmental school at Vitry*, where the pupils number 900. Following vaccination, not one case of diphtheric angina has occurred among the vaccinated pupils, in spite of the presence of many cases in the general population of Vitry. Some of the unvaccinated children fall victims to diphtheria every year.

We also mention the trials of vaccination made at the Seaside Hospital at Berck, from 1926 to 1931, in which M. Mozer and the late G. Mozer were associated with us. With a stable population of 1,000 children, including many exits and entrances, there were at Berck 137 cases of diphtheria, with 12 deaths, before the application of vaccination and during the years 1923, 1924 and 1925. After a period of organization and tentative efforts, during which decline in the diphtheric morbidity was already appreciable, vaccination was formally instituted and its methodical practice may be considered as dating from 1928. During the three years 1928, 1929 and 1930, 10 cases of diphtheria occurred among vacci-

²⁶ M. and G. Mozer. Bull. et Mém. de la Soc. Méd. des Hôpitaux, 44: 1443, 1928.

nated children, including one fatal case in a child whose Schick reaction remained negative in spite of vaccination.

J. Parisot, P. Melnotte and Engel state that, between December, 1927, and September, 1935, only one death from diphtheria occurred among a total number of 6,149 children vaccinated at the preventorium at *Flavigny*, in the French département of Meurthe-et-Moselle. The diphtheric mortality thus remains extremely low (0.16 per 100,000). This fact is not due to any attenuation in the virulence of the Löffler bacillus at the preventorium in question, since in the same département, or territorial division, the average diphtheric mortality for the years 1928 to 1933 was 36 annually, the mortality per 100,000 inhabitants being 6.6. The course followed by the morbidity in this same preventorium is still more striking. In 1927, before vaccination was introduced, it was 10 per cent, declining to 1.4 per cent as soon as vaccination was applied and to 0.47 per cent after immunization became properly checked and controlled. Parisot, Melnotte and Engel declare that the efficacy of diphtheria vaccination is once more brilliantly evident and that it is the only procedure capable of insuring prophylaxis against diphtheria among preventive institutions, even more notably than elsewhere.²⁷

At *Montluçon*, a central city of France, Cleret²⁸ assumed direction of the public health agencies in 1930, and became immediately interested in extending diphtheria vaccination. In entire accord with the local physicians, he organized regular vaccination periods and, between December 1, 1930, and January 1, 1933, a period of two years, he was able to vaccinate nearly two-thirds of the child population, numbering about 4,000 individuals. Epidemiological data were checked in the best possible fashion and supply the following results.

Of 1,492 unvaccinated children, there were 48 clinical cases of diphtheria, of which 30 were verified bacteriologically, the average being 32.12 per 1,000. There were 6 deaths, or an average of 4 deaths per 1,000 unvaccinated children and 12.5 deaths per 100 cases of diphtheria. Among 248 children considered vaccinated incompletely because of receiving less than 30 antitoxic units, 1 clinical case of diphtheria, not verified bacteriologically, occurred in a child receiving a total of 15 units, given in two injections. Among 2,260 children considered satisfactorily vaccinated on receiving 30 to 75 anatoxic units, 6 clinical cases, of which 5 were verified bacteriologically, were observed, or an average of 2.65 per 1,000 vaccinated children. No deaths occurred in this series.

At *Saint-Etienne*, an industrial city of 200,000 inhabitants, diphtheria appeared epidemically for several years. Anatoxic vaccination has been employed in this city since 1928, through the active interest of Poulain,

²⁷ J. Parisot, P. Meinotte and G. Engel. *Rev. d'Immunol.*, 1: 501, 1935.

²⁸ H. Cleret. *Bull. Acad. Méd.*, 110: No. 4, 1934. *Rev. d'Immunol.*, 1: 570, 1935.

Director of the Municipal Bureau of Hygiene. The various articles published by Poulain²⁹ give the details of his campaign against diphtheria, which serves as an example, like the campaign at Montluçon conducted by Cleret. We present only a summary of the results. Since 1931, children of the nursery schools, aged 2 to 6 years, and under medical supervision, have been vaccinated. Some of them received a quantity of anatoxin containing 10 units per cubic centimeter sufficient to provide them with 35 units, though vaccination was incomplete in some of these children. Other children received 40 to 60 units, according to the strength of the anatoxin employed.

In brief, 73 per cent of the children in the nursery schools at Saint-Etienne were vaccinated between 1931 and 1935. In 1934, four-fifths of the vaccinated children received more than 40 anatoxic units. The morbidity was notably diminished, since only 7 cases of diphtheria occurred in 1934 among the 20,000 pupils enrolled in the nursery and primary schools. Among the children vaccinated with more than 40 units of anatoxin, the morbidity declined greatly and the mortality was reduced to zero, in four years. It may be justly said that vaccination has tended to cause diphtheria to disappear at Saint-Etienne, because when diphtheria becomes rare among vaccinated persons, morbidity is lowered among those not vaccinated and the dangers of contagion are consequently less.

In an *entire French département*, that of the Ain, Poncet, departmental inspector of hygiene, estimates the diphtheria morbidity among 48,000 unvaccinated children at 4.16 per 1,000, and that occurring among 12,200 vaccinated children at 0.41 per 1,000, for the year 1934. The mortality for the same year was 0.29 per 1,000 among unvaccinated children, and no deaths occurred among those who were vaccinated. At Marboz, a town of 2,060 people, in this same département of the Ain, 300 of about 360 children were vaccinated, on account of the appearance of 2 cases of diphtheria in January, 1931. No case has occurred among these children since then, but among those not vaccinated there were 1 case in 1931, 3 cases in 1933 and 1 case in 1934.

In France, then, as in other countries, the morbidity and mortality have diminished among various groups, in cities, and in districts and regions, where vaccination against diphtheria has been practiced. The resulting diminution has naturally been of greater or less degree, according to the more or less ideally favorable conditions of applying vaccination, and also according to the immunizing activity and the doses of the anatoxin which was employed.

The value of this method of preventing diphtheria by the use of specific anatoxin has been thus fully confirmed in proportion as its practice has extended. In fact, it is impossible to deny the value of a method which,

²⁹ Poulain. Bull. Acad. de Méd., July 5, 1932. Ann. de l'Inst. Pasteur, November, 1932. Rev. d'Hygiène, 56: No. 6, 401.

when applied to millions of individuals and in every part of the world, has abolished, when correctly and extensively employed, 70 per cent to 90 per cent, and sometimes even more, of the cases of diphtheria among vaccinated population-groups and has reduced the mortality of this frightful pestilence in an equally notable degree, and all this in only a few years. How long a time was required for a similar extension of the Jennerian vaccination against smallpox?

PROGRESS IN THE METHOD

As we have seen, at least 95 per cent of all individuals vaccinated under good conditions may be rendered immune to diphtheria, as judged by negative Schick reactions, by means of an anatoxin measuring 10 units by titration and employed in a total dosage of 30 units by the original technique including three injections, respectively of 0.5, 1, and 1.5 cc., given three weeks apart. In actual practice, and for various reasons, immunity is conferred in 92 per cent, and sometimes only in 90 per cent, of the cases. There may thus remain from 5 per cent to 10 per cent of the vaccinated individuals who are immunized imperfectly, or not at all.

It was evidently necessary, therefore, to diminish or even obviate entirely the number of individuals remaining unimmunized or insufficiently immunized and thus continuing to be susceptible to diphtheria, in spite of being vaccinated. This necessity was especially urgent from the fact that the number of cases of diphtheria *among the vaccinated persons* would tend to increase as the method should extend. In this way, there was danger that the method might appear less effective than it really is. There is a general tendency, in fact, to consider the *absolute*, and not the *relative*, number of the cases of diphtheria appearing in vaccinated individuals. Even a partial failure thus counts against the method, while successes which are many and complete are readily forgotten and the method is not credited with them, as it should be. It must be admitted, too, that a method requiring three injections has certain practical disadvantages which hamper the extension, and therefore the efficacy, of a process designed for general prophylaxis.

As we have said on several occasions, the efficacy and success of a method of immunization employed to prevent a disease like diphtheria really depend upon the production of a high degree of immunity in the larger number of those who are vaccinated, if not in all of them, and also depend upon the facilities available for practically applying the method in view. We have wished to define and provide the conditions most favoring proper vaccination with diphtheria anatoxin. Such has been the object which we have had personally in view, and to which our laboratory studies have been devoted, during the last eight years. The principles prevailing in the elaboration of our method should also serve as guides to any newer investigations which we might undertake.

For animals as well as for man, we clearly proved the fact that, the greater the intrinsic antigenic value of anatoxin as determined by the flocculation test, the greater its immunizing power.³⁰ According to this principle, any improvement in the antidiphtheric immunity conferred by anatoxin depends very largely upon the preparation and use of an anatoxin whose antigenic value is as high as possible. Since anatoxin is produced from diphtheria toxin, the solution of the problem thus stated consists, first, in the preparation of a diphtheria toxin containing many antigenic units.

Increasing the immunizing activity of anatoxin

By continuing to improve bouillons used for cultures, in some cases with the collaboration of A. Berthelot,³¹ we have gradually raised the value of the toxin, at first of 8 units, to a value averaging between 30 and 40 units per cubic centimeter, and even more.³² The anatoxin now prepared from a toxin of the high activity just indicated, and which is supplied by the Pasteur Institute for general use, consequently contains at the present time, 1937, at least 30 units, while the anatoxins first employed for vaccination contained only 8 units per cubic centimeter, as remarked above.

As soon as the antigenic value of diphtheric anatoxin was thus raised and improved, vaccination was immediately and methodically instituted, in order to test the practical value of the new product. This work was promoted in France through the aid of Debré and his associates, by M. and G. Mozer, and by others, while Timbal and Nélis collaborated in Belgium and M. Nicolle contributed to it in Tunisia. The results obtained by these workers³³ showed that two injections, respectively of 1 and 2 cc. and given three weeks apart, of an anatoxin containing at least 20 units, permitted an average increase in the incidence of immunity to from 96 per cent to 99 per cent, while also increasing the value of the immunity acquired by each individual thus vaccinated. The practical application of vaccination was rendered more convenient, since the number of injections was reduced from three to two. We therefore accomplished our object.

³⁰ G. Ramon. *Ann. Inst. Pasteur*, 39: I, 1925; 42: 959, 1928.

G. Ramon and P. Nelis. *Ann. Inst. Pasteur*, 50: 1933.

³¹ G. Ramon. The production of a very active diphtheric toxin. *C. R. de l'Acad. des Sc.*, 139: 178, 1929. G. Ramon and A. Berthelot. *C. R. Soc. de Biol.*, 110: 530, 1932.

³² Pope (*Brit. J. Exp. Path.*, 13: 207, 1932). Pope and Smith (*Journ. Path. Bact.*, 35: 573, 1932) and E. Taylor (*Ann. Inst. Pasteur*, 55: 474, 1935) devised various formulas for culture media permitting the productions of toxins, and consequently of anatoxins, of high antigenic value.

³³ See *Bull. de l'Acad. Royale de Belgique*, 478, 1931; *C. R. de la Soc. de Biol.* 107: 185, 1931; *Bull. et Mém. de la Soc. Méd. des Hôpitaux*, No. 24, July 3, 1931; *Bull. Acad. de Méd.*, 100: No. 37, 1935; *Bull. Acad. de Méd. de Belgique*, 355, 1933; *Bull. Off. Intern. d'Hygiène Publique*, 85: fasc. 8, 1933.

When applied in practice, the improvements obtained still further diminished diphtheria morbidity. At Saint-Etienne, as we have seen, the morbidity among children receiving quantities of anatoxin between 5 and 25 units had already declined, and became still lower among children vaccinated with 40 to 60 units. The mortality, incompletely abolished in children receiving less than 35 units of anatoxin, now became totally abolished in children receiving more than 40 units. The same results occurred at Montluçon. Do not these successes demonstrate in the clearest way the point which we have always maintained, namely, that the diphtheria immunity produced by anatoxic vaccination is directly proportional to the number of units present in the anatoxin, as measured by our flocculation reaction?

Use of an anatoxin of the high antigenic value conferred by 30 units³⁴ has reduced, in France, the number of vaccinal injections from three to two, while imparting to this method a degree of efficacy which is at least as great in the production of immunity and the prevention of diphtheria as that provided by the former method, or perhaps even greater.

The supplementary, or "recall," injection

We point out above that the immunity conferred by diphtheria anatoxin rises to a maximum and may then decline more or less considerably during the months which follow vaccination, the decline being often, though not always, offset by the action of natural immunization. It is also true that, even after vaccination is properly applied, a small number, consisting of 1 per cent to 5 per cent, of the vaccinated persons are immunized insufficiently, while the immunity developed in others borders on the limits of efficacy. A long time ago, we advised, and were finally able to apply in regular practice, a supplementary, or "recall," injection of anatoxin. This injection increases the existing immunity, and usually in a very considerable degree. In this way it enables those who are but incompletely immunized by ordinary vaccination to produce antitoxin in quantities sufficing to protect them against diphtheria. The beneficial action of the supplementary, or "recall," injection has been confirmed by a number of workers, especially including Zdrodowski and Halapine, Madon, and Foa.

³⁴ Foreign investigators have at various times, and again recently, compared the immunity conferred upon human individuals by the anatoxin which we prepare and test with the immunity produced by commercial samples of anatoxin, applied in the countries where these tests have been made. The results have always been in favor of the anatoxin prepared and checked under our direction and prove the value of systematically testing anatoxin by the flocculation reaction. See Claire E. Healey, Journ. of the A. M. A., CV, 1182, 1935, and G. F. and G. H. Dick, Journ. of the A. M. A., XCII, 1901, 1929.

*Associated vaccinations*³⁵

Diphtheria and tetanus vaccinations have been rendered practicable, under the best obtainable conditions, through the discovery of specific anatoxins, and have greatly increased our resources for combating infectious diseases. However, there was a certain risk of singularly complicating the tasks of hygienists, clinicians and those interested in public health by adding anatoxic vaccination to methods already existing, such as vaccination against typhoid. In order to be truly effective, each of these methods requires several procedures, whose successive application would become very complicated. For example, a plan for immunizing nurses, suggested a few years ago in the United States, included no less than twelve injections of different vaccines.³⁶ Were such a preventive program not wholly impossible to apply in practice, there would still be great difficulty in persuading the public to adopt it. In any event, it could not be readily rendered generally applicable.

In order to render the prevention of infectious diseases effectual for individuals and for population groups, it was necessary to simplify the application of immunization methods which the laboratory had placed, or might at some future time place, at the disposal of clinicians and persons interested in hygiene and public health.

Simplification was begun a number of years ago, through the recommendation and practice of vaccinating against typhoid and paratyphoid with a mixed vaccine, as adopted by Castellani and by Widal and Sicard. This vaccine, however, is composed of antigens of the same group and is a mixture of vaccines which are alike in their nature and mode of preparation. Although it might be granted that a single procedure may be capable of immunizing the organism against bacteria which are in some degree related and which act in similar ways, it had appeared impossible hitherto for the same organism to meet the task imposed by the production of several artificial immunizations, induced by a mixture of antigens whose components differ as widely as do those of the antityphoid vaccine and the diphtheria anatoxin, and by an antigenic combination intended to combat diseases whose clinical manifestations differ as distinctly as those of typhoid, diphtheria and tetanus. The production of multiple immunization of this kind was considered impossible because of the theory of "antigenic competition," particularly supported by German writers and generally accepted for some time.

The method of associated vaccinations, established by the late Chr. Zoeller and ourselves twelve years ago, completely upset the theory of antigenic competition. At the same time, it was destined to prove that polyvalent immunization

³⁵ For fuller details, see our recent article. *Ann. de Méd.*, 42: 381, 1937.

³⁶ "An immunization program." *Journ. of the A. M. A.*, XC, 311, 1928.

may be readily realized by means of a mixture of vaccines, such as the typhoid vaccine and the diphtheria and tetanus anatoxins, and that it is very advantageous. Its special advantage is partly due to its convenience in facilitating the practice and extension of combined vaccinations, but is also important because of the increased effectiveness of the antitoxic immunities which it is capable of conferring.

From the theoretical and scientific viewpoint, a brief account of the origin of the principle governing the method of associated vaccinations is not wholly without interest.

Through observations directed to the horses employed for producing antitoxic serum, we announced, as early as 1925,³⁷ that the addition of certain non-specific substances, such as powdered tapioca, to diphtheria or tetanus anatoxin increases the production of antitoxin and consequently confers upon the test animals a higher degree of immunity. Tapioca may be replaced by alum (Glenny), calcium chloride, lanolin and a number of other substances, as we and our associates have shown.³⁸ However, most of these substances cannot well be employed with human individuals, on account of the rather severe reactions which they may produce. These facts suggested to Zoeller and ourselves that a mixture of anatoxin and a bacterial vaccine, like the typho-paratyphoid vaccine, might serve the purpose.

To these mixtures, composed of two antigens differing as widely in nature as do an anatoxin and a bacterial vaccine of the T. A. B. type, or consisting of anatoxins whose specificities are as wholly unlike as those of the diphtheria and tetanus anatoxins, for example, Zoeller and ourselves applied the term "*associated vaccines*."³⁹ The results of our first trials of the associated vaccines satisfied our expectations.⁴⁰ For example, they showed that, as a very general rule, the Schick reaction becomes negative in 100 per cent of the individuals receiving three injections of an associated vaccine containing diphtheria anatoxin and the typho-paratyphoid vaccine.

Studying associated diphtheria and typhoid vaccination as practiced in the French army, Dopfer observed that the Schick reaction becomes negative in 100 per cent of the soldiers vaccinated in this way.⁴¹ Loiseau and Laffaille⁴² have recently presented the results obtained through

³⁷ G. Ramon. Bull. de la Soc. Cent. de Méd. Véter., 101: 227, 348, 1925.

³⁸ See the Revue d'Immunologie, 3: 193, 202, 285 and 389, 1937.

³⁹ Associated vaccines containing an anatoxin and a bacterial vaccine or a mixture of anatoxins. C. R. de la Soc. de Biol., 94: 106, 1926.

⁴⁰ G. Ramon and Chr. Zoeller. Bull. Acad. de Méd., 95: No. 5, 1926. Presse Méd., No. 31, 1926.

⁴¹ Ch. Dopfer. Bull. Acad. de Méd., 104: 794, 1931, 105: 1932. Ann. Inst. Pasteur, 50: 1933.

⁴² G. Loiseau and A. Laffaille. Report, Congress on Hygiene, Paris, October 19-22, 1936.

ten years of practical experience with associated diphtheria and typho-paratyphoid vaccination. They have shown that, of 466 adults vaccinated in this way, 462, or 99.15 per cent, presented Schick-negative reactions six weeks after the final injection.

Associated vaccinations have been in practical use in France for several years. At the present time, the following types of them are employed. *Diphtheria and tetanus*, employing a mixture of the two specific anatoxins.

Typho-paratyphoid and diphtheria, in which the T. A. B. vaccine and diphtheria anatoxin are combined.

Typho-paratyphoid, diphtheria and tetanus, the mixture for injection containing the T. A. B. vaccine and the diphtheria and tetanus anatoxins, etc.

Associated diphtheria and typhoid vaccination has been very extensively practiced in the *French army* since the beginning of 1930. The method was first inscribed and recommended in a law dated December 21, 1931, rendering vaccination obligatory in all garrisons, military and naval stations, and the like, in which diphtheria may occur endemically. A new law, dated August 15, 1936, made associated diphtheria, tetanus and typhoid vaccinations, obtained by giving three injections, two weeks apart, of a mixture of diphtheria and tetanus anatoxins and typhoid vaccine, obligatory for the French army.

Since the practical value of associated vaccinations has been amply confirmed by regular use among a wide variety of population groups and among children and adults, this method has been extending widely, especially in France, since its introduction. It permits the production of several immunizations by a single series of procedures, which are of very high practical convenience. The immunities produced are mutually reinforced and successful results are thus rendered certain. This method may be considered the method of choice, appearing most opportunely for permitting the simultaneous prevention of several of the gravest of the various infectious diseases affecting man.

Are further improvements still possible? Following the various studies and investigations conducted up to this time, vaccination at a single application and produced by a single injection has been recommended in certain countries, through the use of these anatoxins, which are concentrated and whose immunizing activity is reinforced by various technical methods. The form of vaccination thus suggested is more or less known as the "one shot" method.

Attempts at vaccination by a single injection

Critical study

The practice of vaccination by a single injection is very attractive at first view. It is true that interesting results obtained by injecting single

doses of anatoxins which are concentrated or treated with alum have been published by various writers, among whom are Claus Jensen,⁴³ Volk,⁴⁴ Isabolinski and his associates,⁴⁵ Farago,⁴⁶ Sordelli and others,⁴⁷ Melnik and others,⁴⁸ Wells, Graham and Havens,⁴⁹ Walker,⁵⁰ Naughteen, White and Foley,⁵¹ and still others.

However, results which seem far less satisfactory have been presented by White and Schlageter,⁵² and Pansing and Shoffer,⁵³ in the United States; Lai⁵⁴ and Judd,⁵⁵ in China; FitzGerald,⁵⁶ McKinnon and Ross,⁵⁷ Fraser and Halpern⁵⁸ and Schuchardt and Cook,⁵⁹ in Canada; McSweeney,⁶⁰ Parish,⁶¹ Powell⁶² and Williams, Dear and Stewart,⁶³ in Great Britain; and various other writers do not favor the single injection method.

Fraser and Halpern studied individuals vaccinated with a single injection of an anatoxin treated with alum. They find that only 62 per cent of the serums of these individuals contained more than 1/100 unit, ten weeks after receiving the single injection, although this quantity occurs in the serums of at least 91 per cent of the persons who receive three doses of anatoxin not treated with alum. Again, the same proportion of anatoxin (1/100 unit) occurs one year after vaccination in 91 per cent of the serums of those who receive the classical three injections, but was present in this study in the serums of only 19 per cent of the individuals receiving a single dose of alum-treated anatoxin and examined one year after the single injection. *The immunity conferred originally by the single injection had therefore considerably declined.*

⁴³ Claus Jensen. C. R. Soc. de Biol., 108: 528, 1931.

⁴⁴ Volk. Am. Journ. Public Health, XXV, 430, 1935.

⁴⁵ Isabolinski, Judenitsch and Lewzow. Zeitschr. f. Immunitäts, 65: 218, 1935.

⁴⁶ Farago. Medez. Welt., 10: 13, 1936.

⁴⁷ Sordelli, Savino and Ferrari. Rev. Inst. Bact., Argentina, 6: 687, 1935. Folia Biologica, 269, 1936.

⁴⁸ Melnik, Krassnov, Palant and Khorouzenko. Ann. Inst. Metchnikoff, 4, 1936.

⁴⁹ Wells, Graham and Havens. Am. J. Public Health, 22: 648, 1932.

⁵⁰ Walker. Journ. of the A. M. A., CII, No. 12, 1934.

⁵¹ M. Naughteen, J. H. White and A. Foley. Med. J., 898, 1935.

⁵² John White and E. Schlageter. J. A. M. A., 915, 1934.

⁵³ H. N. Pansing and E. R. Shoffer. Am. J. Public Health, 26: 786, 1936.

⁵⁴ D. G. Lai. Chinese Med. J., 49: 340, 1935.

⁵⁵ F. H. Judd. Chinese Med. J., 49: 826, 1935.

⁵⁶ J. G. Fitzgerald. Canad. Pub. Health J., 27: 23, 1936.

⁵⁷ N. E. McKinnon and Mary A. Ross. Journ. of the A. M. A., 105: 1935.

⁵⁸ D. T. Fraser and K. C. Halpern. Canad. Pub. Health J., 26: 409, 1935.

⁵⁹ C. T. Schuchardt and E. B. M. Cook. Canad. Pub. Health J., 27: 278, 1936.

⁶⁰ McSweeney. Brit. Med. J., 103, 1935.

⁶¹ H. J. Parish. Brit. Med. J., 209, February 1, 1930.

⁶² A. Powell. Brit. Med. J., 736, 1936.

⁶³ H. C. Maurice Williams, J. B. Dear and W. Stewart. Brit. Med. J., 1078, 1936.

Parish noted that Schick reactions proved to be negative, five weeks after vaccination with a single injection of anatoxin precipitated with alum, in only 51 per cent of the vaccinated children.

Collaborating with G. Loiseau and A. Laffaille, we have recently tested the results produced by a single injection of an alum-anatoxin (method of Sordelli), applied to about one hundred children having Schick-positive reactions. After the single injection, the Schick test was negative in scarcely 50 per cent of these children.⁶⁴

Among children previously vaccinated with alum-anatoxin, Schröder, of New York, found the Schick test positive in 18 per cent 6 to 12 months, in 23 per cent 1 to 2 years, and in 14 per cent 2 to 3 years, after vaccination.⁶⁵

Julius Blum, also of New York, applied the Schick test to 239 children vaccinated with a single dose of alum-anatoxin. Of this group, 26 per cent ceased to be immune 9 months, 40 per cent in 1 to 2 years, and 82 per cent in 2 to 3 years, after vaccination. On the other hand Blum observed another group, of 103 children, vaccinated with two injections, two weeks apart, each injection being of 1 c.c. of an unmodified anatoxin. Immunity ceased in a period of 1 to 2 years only in 7.5 per cent of these children, of whom every one, without exception, remained immune after periods ranging from 2 to 3 years. Both Blum and ourselves emphasize the importance of these facts.

Consideration of the results of the detailed and systematic investigations by White and Schlageter, McSweeney and others, is not very convincing concerning the superiority of the immunizing value of alum-treated anatoxin. Some writers, including Pansing and Shoffer and Maurice Williams, Dear and Stewart, have recently warned hygienists and physicians against undue enthusiasm in favor of vaccination as applied by the method of the single injection, or "one shot." Especially is this warning timely from the fact that these writers state that alum-treated anatoxin possesses certain disadvantages, such as its tendency to produce reactions which are often severe.⁶⁶

After an experience of two years with many trials made at Southampton, Maurice Williams, Dear and Stewart conclude as follows: in view of the favorable reception accorded the single dose by physicians, they should

⁶⁴ These tests are reported here for the first time.

⁶⁵ Schröder and Julius Blum, cited by William H. Park. *Journ. of the A. M. A.*, CIX, No. 21, 1683, 1937.

⁶⁶ These reactions consist of edema, abscess at the injection site, fever and other effects. A. L. Shafton, *J. Pediat.*, 8: 676, 1936. Fred H. Judd, *Chinese Med. J.*, 49: 826, 1935. Lillian Rositzka. *J. Pediat.*, 7: 662, 1935. Also others. After a certain number of trials, P. Nelis and ourselves directed attention some time ago to the marked reactions produced by anatoxin treated with calcium chloride and ceased to apply this combination to the vaccination of children. *C. R. Soc. de Biol.*, 109: 57, 1932.

fully understand the uncertainty attaching to its primary efficacy and to the duration of its effects. This uncertainty has been already noted in the United States,⁶⁷ concerning modified forms of anatoxin. In this connection a dilemma arises, concerning human individuals but not at all referring to animals. In alum-anatoxin, either the proportion of alum may be large enough to increase the immunizing activity of anatoxin while producing reactions which are so severe that they largely impair the utility of the vaccine, or the proportion of alum is low, in which event immunity is increased very slightly, or not at all, by the added alum.

In Toronto, FitzGerald based his observations upon experience acquired in the course of vaccination very extensively applied by our technique, more than one million individuals having been vaccinated in this way in Canada during the past twelve years, with the success which has become well known.⁶⁸ *He concluded that, in spite of opinion favoring the single injection of an alum-anatoxin, he remains convinced that the three conditions which should be fulfilled by a diphtheria vaccine, namely, harmlessness, high immunizing activity and the assurance of durable protection, are met most satisfactorily by vaccination with two or three doses of anatoxin, not concentrated, not treated with alum, and of high flocculating activity, given three weeks apart.*

After recently showing⁶⁹ the doubtful results obtained at New York with single doses of alum-anatoxin, William H. Park remarks, *"I think the Department of Health of the City of New York is wise to be conservative and go back to a standard of two doses of toxoid, either fluid or alum precipitated.*

Still again, a recent circular issued by the Minister of the Interior of Germany and Prussia⁷⁰ states in particular, and in accordance with the results of many tests, that sound and durable immunity is obtainable only by means of *two injections*, one month apart, of diphtheria vaccine titrating at least 30 units (S. E.), or by three injections of any vaccine whose value is below 10 units. Does not this statement constitute still another confirmation of the method which we have established and of the teaching which we have always maintained?

Concerning vaccination as accomplished by the single injection, we take the liberty of repeating here what we have already said on many occasions. *Under no pretext should the efficacy of a method of vaccination be sacrificed in favor of mere facility of practical application. It is imprudent, if not dangerous, to provide a large number and large proportion of vaccinated individuals with no genuine security. In the present state of our knowledge, use*

⁶⁷ J. A. M. A., 105, No. 11, 889, September, 1935.

⁶⁸ G. Fitzgerald. Internat. Congress on Microbiol., London, 1936.

⁶⁹ William H. Park. Journ. of the A. M. A., 109, no. 21. 1683, 1937.

⁷⁰ Special circular of October 2, 1937. Reich-Gesundheitsblatt, November 10, 1937.

of the single injection appears to us an expedient, whose principal advantage consists of ease of application. It is attractive and tempting, but it risks the occurrence of unfortunate and unwelcome surprises.

It has been claimed that the inhabitants of some countries, which, by the way, are very few, do not ardently welcome a method of vaccination requiring two or more injections and that it would therefore be better to vaccinate with a single dose than not to vaccinate at all. We consider this opinion an error. To permit individuals vaccinated in this imperfect way to believe that they are rendered refractory and resistant to diphtheria, whereas only 50 per cent of them are immunized (Fraser and Halpern, and Parish), and whereas 80 per cent of them regain susceptibility to diphtheria one year after vaccination by the single injection, or "one shot," is to assume an extremely grave responsibility. These individuals, thus defenseless, may readily contract diphtheria. If they fail to receive antitoxin, or diphtheria serum, because they are mistakenly considered immune, some of them may die of the disease. Is there anyone who would care or dare to take the responsibility of recommending and propagating the method of the single dose, which exposes the public to such undesirable effects? Is it not quite enough to be obliged to take into account imperfections and failures, which are inevitable in some degree and which cannot be foreseen or averted, accompanying a method which, nevertheless, imparts sound and satisfactory immunity to the great majority, if not to all, of those who are vaccinated in accordance with its principles?

It has been recently proposed (Jensen, of Copenhagen) to offset and correct the lack of efficacy of the "single injection" by supplementing it with nasal instillations of anatoxin according to the method of "anatoxic rhino-vaccination" devised by Chr. Zoeller and ourselves as early as 1927.⁷¹ As we distinctly stated, however, this method is neither sure nor practical and its application must be carefully supervised. We therefore recommend it only in special and unusual cases, as when an individual has shown particular sensitiveness when receiving a subcutaneous injection of anatoxin. In brief, two modes of immunization are of very uncertain efficacy. On the one hand the "one shot" method, and on the other hand the "nasal instillations," are by no means sure of conferring immunity.

Whatever the value of the antigen employed, the method of the single injection fails to take into account the well established and well known stimulating action exerted by a second injection. Again, it controverts the principle which we have firmly adopted, namely, that *the efficacy of a method of*

⁷¹ G. Ramon and Chr. Zoeller. C. R. Soc. de Biol., 96: 757, 1937; Bull. Acad. de Méd., 97: No. 26, 1927; Presse Méd., No. 69, 1049, 1927. A. Della Vedova confirms the point established by us, that immunity imparted by the nasal route proceeds from general immunity and that it is inferior to the immunity obtainable subcutaneously. Boll. S. S. M., No. 1, 80, 1937.

immunization and collective prevention is inseparable from the production of a high degree of immunity in the larger number, if not in all, of those who are preventively vaccinated.

In the present state of our knowledge, anatoxic vaccination should be applied according to the technique which we have defined, whose efficacy has been confirmed by the results which it has produced in very many of the countries of the world. The technique just mentioned is indicated below.

Three injections of anatoxin are required with anatoxins whose value does not exceed 10 units. In no event should the anatoxic value be below 6 units.

Two injections may be employed, respectively of 1 and 2 cubic centimeters, if the value of the anatoxin employed is equal to, or exceeds, 30 units per cubic centimeter.

Intervals between injections should never be less than two weeks. *For a maximum of efficacy and practical convenience, intervals are preferably of three weeks.*

For reinforcing and enhancing the sureness and duration of immunity, vaccination may be completed by a *supplementary, or "recall,"* injection, given one year after regular vaccination.

Whenever possible, simple anatoxic vaccination should be replaced by the *method of associated vaccinations*. This procedure combines, in a single series of three injections, different vaccines, such as the anatoxins of diphtheria and tetanus and the antityphoid vaccine, and in this way confers immunity against several diseases, *while at the same time increasing the efficacy of each specific immunization.*

CONCLUSIONS

Diphtheria anatoxin first appeared in 1923, following studies of the phenomenon of flocculation, continued since the date just mentioned. Practically, anatoxin is obtained by the combined action of formalin and heat upon a specific toxin. It constitutes a harmless, stable and irreversible vaccine, whose antigenic activity is readily appreciable and measurable in vitro by means of the flocculation reaction, and is capable of producing in man the appearance and development of an active, sure and durable immunity.

The results accomplished since 1923, first of all in France and then in practically every country, and with many millions of human individuals, have firmly established the efficacy of vaccination with the diphtheria anatoxin, which is continually being rendered still more effective by progress and improvement in laboratory methods.

These results have confirmed the sureness and soundness of the principles which have governed the elaboration and perfecting of this method of immunization and which have still later served as guides to further improvements in it.

They compel the conviction that diphtheria may be caused to disappear through the systematic practice of this method of prevention. Up to the present time, this method has permitted a reduction, usually very considerable, in the morbidity and mortality of the epidemic disease known as diphtheria, wherever it has been correctly and judiciously applied.

The present universal application of anatoxic vaccination notably emphasizes the great value and merits of the test discovered, twenty-five years ago, by BELA SCHICK.

THE SKIN REACTION WITH DIPHTHERIA TOXIN ON HUMAN BEINGS AS A TEST PRECEDING THE PROPHYLACTIC INJECTION OF DIPHTHERIA SERUM

PRIVATDOZENT DR. B. SCHICK

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This is a translation of the original article which appeared in 1913 in the *Muenchener Medizinische Wochenschrift*.

It is republished at this time to commemorate the twenty-fifth anniversary of the announcement by Dr. Schick of his significant observations which, since then, have paved the way for the development of protective measures to block effectively the inroads of a menacing disease against which hitherto there was no adequate defense.

In recognition of the great service he thus rendered to humanity, Dr. Schick was recently awarded the Gold Medal of the New York Academy of Medicine (March 3, 1938) and the Addingham Gold Medal by the authorities of Leeds University, England (April 12, 1938).

Editor

The investigations of Loos, Karasawa and Schick et al. show that children suffering with diphtheria, examined before the injection of antitoxin, do not possess diphtheria antitoxin in their serum. The examination of such children in the last years by Busacchi, Kassowitz and myself give the same result.

The prophylactic injection of diphtheria antitoxin should supply the missing antitoxin. According to the investigations of Wasserman, Fischl and v. Wunehheim, Abel, Orlowski, Karasawa and Schick, Hahn, Groer and Kassowitz, and Kleinschmidt, many individuals possess antitoxin in their serum without having shown during their life any symptoms of diphtheria. Eighty per cent of newborns show such antibodies, of adults up to 90 per cent and of children 50 to 60 per cent (Magyar and Schick). One could, therefore, omit the injection of antitoxin in many instances if there existed a method of determining the presence of antitoxin in the serum. The old methods are not satisfactory. Roemer's method of testing the guinea pig intracutaneously is an important step forward, but it is too complicated and too expensive, as guinea pigs have to be used. Loewenstein, Michiels and Schick could prove that intracutaneous injection of minimal amounts of diphtheria toxin produces a specific inflammatory reaction at the site of the injection.

For this injection a regular record syringe of one ccm. with ten partitions is needed. The most important part is the needle. The latter must be very thin and its point very short so that after introduction of the needle

into the uppermost layer of the skin the opening of the needle pointing upward is covered as easily as possible. The amount of injected fluid should be .1 c.c. of a toxin solution, the strength of which must be determined for each batch of toxin. As a rule, the effective dose is equal to 1/50 of a single lethal dose for a 250 g. guinea pig; for instance, if the single lethal dose is 0.005 grs. for 250 g. guinea pig, .1 of a dilution of 1:1000. If the injection is made correctly a white wheal with punctations is seen immediately. This design is due to the presence of the opening of the hair follicle.

The reaction developing at the site of the injection of the toxin, very much resembles in the first twenty-four to thirty-eight hours a positive Tuberculin reaction. Four to eight hours after the disappearance of the traumatic reactions, gradually increasing redness and infiltration (10-25 mm. diameter) develop. Usually the maximum is reached after forty-eight hours, the reaction lessens under pigmentation and slight desquamation. But the quality of the redness is different from the Tuberculin reaction. The redness is brighter. In case of great intensity the inflammatory reaction increases, particularly in the centre. The skin becomes blistered, gelatinous and shrivelled. Pigmentation and desquamation follow. I did not encounter more intensive reactions. The necrosis described by Bingel is due to the enormous dose of diphtheria toxin. Frequently a brighter red halo develops around the central infiltration within twenty-four to thirty-six hours. This halo disappears in the following twenty-four to thirty-six hours without leaving any pigmentation. Later on, only the central reaction is visible by its pigmentation, and the size of the original reaction may be measured by the diameter of the pigmented area of the skin. The negative result of the test proves the presence, in the serum, of protective antibodies against diphtheria toxin in an amount sufficient for prophylaxis. The positive result of the test does not prove with certainty the lack of such antibodies, because some individuals, children and adults, show inflammatory reactions at the site of the injection, although antibodies may be present in the serum. Although such inflammatory reactions are not the effect of the diphtheria toxin proper, but are possibly an hyper-ergic reaction to protein substances present in the diphtheria solution, it is sometimes difficult to differentiate such "pseudoreactions" from the original reaction due to the diphtheria toxin proper. On account of these exceptions, decisive conclusion about the presence of antibodies should only be drawn if the test is negative.

I mentioned before that the presence of antibodies in the serum is incompatible with the presence of a fresh diphtheria disease. So we may expect that children suffering with diphtheria react positively to the test if this test is applied before the injection of diphtheria antitoxin. This is always the case. A negative test in doubtful cases of diphtheria speaks against diphtheria. I point out that among nurses tested with diphtheria antitoxin only positive reactors come down with diphtheria.

An exception exists in case of malignant diphtheria (Busacchi, Kassowitz, Schick). Also, extremely cachectic individuals are unable to react positively to diphtheria toxin. v. Groer and Kassowitz found negative reactions in 10 per cent of newborns, in spite of the absence of antitoxin, which may be explained by a lowered ability of the skin of the newborn to react.

I have previously pointed out that the test with diphtheria toxin reveals the susceptibility to diphtheria. If the testing should lead to a reduction of prophylactic serum treatment against diphtheria, we must be able to prove that the percentage of negative reactors is large enough. Information can be achieved by a statistical survey of the results of the test arranged in age groups.

These figures taken from the investigation of Magyar, Michiels and Schick, and v. Groer and Kassowitz, are the following:

	<i>Total</i>	+	-	
Newborn.....	291	16	275	= 93%
1 year.....	42	18	24	= 57%
2-5 years.....	150	95	55	= 37%
5-15 years.....	264	131	133	= 50%

Newborn, who possess antitoxin in 84 per cent and show a negative test in 93 per cent, need no prophylactic treatment in most cases. This statement agrees with the clinical experience (Schlichter) that newborns rarely acquire diphtheria.

Our experience is that the frequency of negative tests diminishes from the second month of life and reaches about 50 per cent in the first year. In this period 50 per cent of the children need no prophylactic treatment. In the next period 40 per cent show negative reaction. Towards the end of childhood again 50 per cent are reached. After that the number of negative reactions probably increases further. We see that during childhood and even in the period between two and five years a considerable number of individuals need no prophylactic injection with serum.

It could be stated that the state of immunity of an individual may change, especially under the influence of certain diseases (influenza, measles, etc.). As far as measles is concerned, Karasawa and Schick were not able to find any change. But it should be admitted that other diseases may have such an influence. The reaction remains unchanged within four weeks. In order not to overlook the loss of antibodies, it may be advisable to repeat the test in institutions once every month in case danger of infection persists. For institutions such as hospitals, military barracks, and boarding houses for children, testing has a practical value. Our procedure is the following: If a case of diphtheria develops, all persons are tested with diphtheria toxin. Twenty-four to forty-eight hours later the test is read. The positive reactors are injected with serum; the negative reactors not. Thus we spare many individuals the injection and the sensitization with horse serum. This is also an economic saving, as the use of large amounts of diphtheria serum is expensive.

A CASE OF PRIMARY BRONCHO-PULMONARY ASPERGILLOSIS

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[From the Medical Service of Dr. B. S. Oppenheimer]

Aspergillus infection in man is interesting not only for its relative rarity but particularly for shedding some light on certain problems of parasitism and saprophytism. Of the many species of the mold only a few are regularly pathogenic. Aspergillus fumigatus is the best known and is one that affects by preference the broncho-pulmonary tissue. It is classed as one of the filamentous fungi (Table 1) and is practically ubiqui-

TABLE 1

Classification of Fungi Which May Produce Lesions Simulating Pulmonary Tuberculosis (Castellani (1))

(1) "Yeast-like" fungi.....	{	Blastomyces
		Cryptococcus (torula)
		Saccharomyces
		Monilia
		Endomyces
(2) Filamentous fungi		
(a) Slender type.....	{	Nocardia
		Anaeromyces
		Vibriothrix
(b) Larger type.....	{	Oidium
		Hemispora
(c) Types with characteristic conidial structures, fructifications, etc.....	{	Aspergillus
		Penicillium
		Mucor
		Rhizomucor
		Acrimoniella
		Sporotrichum
		Acladium

tous in nature. It is a regular inhabitant of the soil, at least in America, and is one of the most abundant molds encountered (2). It has been frequently isolated from cereal products, unmilled grain, hay, and other stock feeds. As an agent of disease it selects for its victims chiefly certain species of birds, particularly the pigeon, but also canaries, penguins, ducks, and chickens (3, 4, 5, 6). Among mammals, dogs and cats are said to be

insusceptible to its spores (7), but lesions have been produced experimentally in rabbits, guinea pigs, monkeys, and others (3, 4).

The majority of writers support the view that, so far as man is concerned, healthy individuals are relatively immune to aspergillus (8). It could hardly be otherwise if the race were to survive, in view of the boundless opportunity for contact with this organism in nature. Indeed, spores of *Aspergillus fumigatus* have been demonstrated in the saliva and nasal mucus of many healthy individuals picked at random (4). Accordingly, the fact of the existence in man of disease caused by this organism must lead one to inquire into the possibility of particular predisposing conditions.

The classic instances of pulmonary aspergillosis in man are recorded in certain occupations which involve prolonged and intimate contact with grains or with birds. Farmers, feed-mill workers, and threshers are prone to this infection. The most frequently quoted example is that of the pigeon-stuffers of the suburbs of Paris who with their own mouths cram the beaks of the birds with a mixture of grains and water, many workers averaging from four to six thousand such gavages a day. Some of them develop a rather severe type of mycotic pseudo-tuberculosis under the double hazard of infection from the grain and from infected birds (3).

Certain dusts are important sources of infection, such as that produced by sponge-cleaners who beat the dried sponges, and by the wig-makers of Paris who comb the hair with rye meal to remove its fat, the air in some of these establishments being practically unbreathable (4). In all these instances one is forced to admit that massive dosage, often repeated, is the principal factor in the pathogenesis of the disease. Symptoms of infection in such cases may be long in making their appearance, and, even in cases severely afflicted, may disappear completely upon removal of the patient to another environment and occupation.

Under other circumstances the factor of constitutional or of local predisposition is the determining one, and from this has sprung the concept of *secondary aspergillosis*. Uncontrolled diabetes has been cited as predisposing to pulmonary aspergillosis with massive necrosis of the lung (9). Concurrent tuberculosis and aspergillosis of the lung is sufficiently important from many standpoints to deserve consideration in a chapter by itself (10). Fuerbringer (11) lists carcinoma, dysentery, enteritis, cirrhosis of the liver, and sepsis as additional predisposing factors. Grippe in a subject with latent pulmonary aspergillosis has been shown to excite a rapidly advancing necrotizing lesion (12).

Nature has thus furnished a nicely balanced experiment in which every conceivable gradation from relative saprophytism to a most virulent parasitism is the exact resultant of two conflicting factors, the dose or virulence of the micro-organism, and the resistance of the host.

In the clinical description of pulmonary aspergillosis two rough groupings

may be employed, a "superficial" form and a "deep" form. In the former are included cases of bronchitis, catarrhal or asthmatoïd, which run a fairly benign course. The "deep" or ulcerative type depends on the ability of the endotoxins of the mold to cause necrosis of lung tissue analogous to caseation as in tuberculosis. These distinctions between the two types are relative and vary also with the degree of the allergic component of the inflammatory response of the tissues or their disposition to undergo fibrosis. Certain apical or basal pleuropulmonary infiltrations of the lung, usually diagnosed as "arrested sputum-negative tuberculosis," and possibly also certain cases of miliary calcifications of the lung (13), may represent a milder intermediate type.

Asthma due to molds. Chronic bronchitis unrelated to sinusitis or to any other obvious cause may be the sole clinical representation of aspergillosis of the "superficial" form which probably includes many instances of the *asthmatic* type. In these the organism exhibits no destructive tendencies in the tissues, and its foothold at best is a very superficial one; in fact, it is just adequate to provide contact of its proteins with the sensitized bronchial mucosa. In contrast to other forms of aspergillosis in which skin tests may evoke a delayed but prolonged cutaneous reaction of the tuberculin type, the asthmatic type exhibits an immediate, transient wheal reaction like that of pollen sensitivity. Van Leeuwen (1925) (14) in Holland was one of the first to point the way in fungus allergy, followed by Hansen (15) in Germany, and by Bernton (16), Brown (17), Hopkins (15), Flood (18), Feinberg (19), and others in this country. Van Leeuwen's studies include data on the surprisingly high incidence of yeasts and molds of various types in the sputum not only of asthmatics but of persons suffering with common cold, influenza, and ordinary bronchitis. In most cases these are undoubtedly non-pathogenic implants in a favorable terrain. In some cases, particularly in allergic asthma, *Aspergillus fumigatus*, as well as other molds, establish themselves as contributory or principal allergenic factors as shown by high sputum counts and positive skin tests. In asthma the skin tests are positive in 40 per cent, in tuberculosis in 15 per cent, while normals are all negative. The source of the mold in each case is not clear, van Leeuwen failing to find them in the air of fields or houses, but implicating rather the stuffing of mattresses and human scalp dander. In this country, on the other hand, the spores of molds are frequent in the open air and may actually exceed the pollen count in summer, when warmth and dampness favor the growth of molds and thereby count for a significant proportion of so-called seasonal asthma in addition to that caused by pollen (19). Asthma related to environment is at times associated with sensitivity to aspergillus, as in persons living in cellars (16). Iodides may be of great benefit, as in Wahl's patient (20), a woman of 39, whose asthma appeared a few hours after she had brushed a heavy growth of mold (*Aspergillus flavus*) from a pair of damp shoes.

Pseudo-tuberculosis. Among the "deep" or ulcerative types of aspergilline bronchomycosis, cases exist in which the lesions progress sluggishly over many years much in the manner of tuberculosis ("pseudo-tuberculosis aspergillina"). The pigeon-stuffers mentioned above furnish the most typical examples. In milder cases the lesions assume a granulomatous character and eventually heal by fibrosis. In some of them, however, tubercle bacilli eventually appear in the sputum (4) and lesions of progressive tuberculosis supplant those of aspergillosis in rather striking analogy to the silicotuberculous complex of stone cutters (21).

More active forms of pulmonary aspergillosis present cavitation similar to that of tuberculosis or suppurative bronchiectasis. At times a caseous pneumonia of fungous origin initiates the picture and undergoes progressive necrotization. In rapidly advancing cases liquefaction, sequestration and cavity formation involve large areas of the lung and death occurs early. There is often considerable inflammatory pleural thickening like that seen in actinomycosis. These more acute forms are almost always secondary, i.e. complications of carcinoma, diabetes, and other debilitating states (22).

The significance of the aspergillus in pulmonary tuberculosis is not yet entirely clear. One should certainly heed Castellani's warning (1) that the mere presence of aspergillus and similar fungi in the sputum cannot be accepted as final evidence in establishing the diagnosis of primary bronchomycosis, but that every possible investigation must be carried out to exclude tuberculosis. Unfortunately for this purpose we cannot depend upon the tuberculin test because of cross sensitization between infections caused by the tubercle bacillus and the aspergillus (10). According to Lapham, tuberculin has no diagnostic value whatever in their differentiation. This may also have important biological significance. The danger of activating latent tuberculous foci by introducing tuberculin into the body is too well known to require further comment. How important aspergillus toxins may be in lighting up a latent tuberculosis cannot be fully judged at present because of inadequate data. The fact must be borne in mind that aspergillus is reported to be capable of sensitizing the body tissues to tuberculin (10), also that clinical tuberculosis may supervene upon primary infection with aspergillus as in the observation already cited (4). However, in the great majority of cases of concurrent aspergillosis and tuberculosis the mold undoubtedly is merely a secondary invader in a predisposed tissue (22). In any event a dangerous symbiosis probably exists. Furthermore, treatment by iodides is contra-indicated because of the presence of tuberculosis. The need for further study of this problem is quite obvious, and more frequent, if not routine tests for aspergillosis should be urged in cases of suspected and proved tuberculosis.

Treatment of aspergillus infection of the lung. The use of fairly large doses of iodides whenever possible has proved of great value. Change of

environment and occupation is clearly indicated when a causal relationship to the disease can be demonstrated and, perhaps, empirically as well. Desensitization by allergenic extracts of the mold may be useful in cases of the asthmatic type (19). Treatment of any underlying constitutional debility is of extreme importance; unfortunately in most instances in which it plays a part the debilitating condition in itself is of hopeless type and the secondary aspergillosis merely plays the part of terminal infection.

ILLUSTRATIVE CASE

The following case conforms to the mild "superficial" type of infection.

History (H. N. Adm. 376473). An electrician, aged 50, entered the hospital on February 15, 1935. For the previous three weeks he had had a dry cough which had lately become productive of yellowish sputum. He had had mild fever, frequent sweats, loss of appetite and weight, and for the last four days had been unable to work.

Examination. Signs of bronchopneumonia were noted in both lower lobes posteriorly, viz. moderate dullness and numerous moist râles. His temperature was normal. His leucocyte count was 12,400 with 61 per cent polymorphonuclear neutrophils. Roentgenograms showed evidences of bronchopneumonia of right and left lower lobes with unusually marked pleural thickening. Sputum tests for tubercle bacilli were negative. The Von Pirquet test was positive (one plus). Numerous dark green particles were detected in the sputum and organisms suggestive of aspergillus were found on smear. A culture of the sputum yielded aspergillus (type not determined), streptococcus viridans, diphtheroids, micrococcus catarrhalis, micrococcus pharyngis siccus, and staphylococcus albus; no pneumococci or tubercle bacilli were recovered. Dental examination disclosed poor oral hygiene, hard gray calcific deposits on the posterior teeth, much repair and crowned teeth. On March 4 he was subjected to bronchoscopy: the bronchial mucosa was found to be very pale, slightly moist, but without exudate.

Course. The patient was given iodides by mouth, and shortly afterward allowed to leave the hospital. Under observation in the Follow-Up clinic he has shown progressive improvement. Nine months following his discharge from the hospital roentgenograms of the chest showed almost complete resolution of the pneumonitis but the marked thickening of the pleura persisted. At the last observation, February 15, 1937, exactly two years after he was first seen at the hospital, an examination disclosed negative physical findings. His only complaint was fatigability. Cough and expectoration had subsided completely. Roentgenograms showed almost complete disappearance of the pleural exudate.

COMMENT

The diagnosis of aspergillosis was quickly made in this case because of the appearance of the patient's sputum. This is a point of great practical

importance. With the unaided eye even the inexperienced observer may detect colonies of fungi in the sputum of these patients, usually as scattered light or dark specks. In some conditions, particularly in actinomycosis, gritty or sandy particles may be detected, at times by the patient himself during expectoration.

The source of infection in this patient was not discovered, but one may easily infer that it lay in the damp and dusty conditions of his work as an electrician. The favorable response to iodide therapy may be cited as evidence that the aspergillus was the primary cause of the pulmonary lesion, although this is no absolute test. It is worthy of note that each of the organisms recovered in sputum culture besides the aspergillus is of a type generally considered to be of relatively low virulence if any (*Streptococcus viridans*, diphtheroids, *Micrococcus catarrhalis*, *Micrococcus pharyngis siccus*, and *Staphylococcus albus*). The occurrence of such a profusion of low-virulent forms suggests that conditions in this patient's bronchial mucosa were favorable, perhaps unusually favorable, for the growth of organisms of low pathogenicity.

SUMMARY

Broncho-pulmonary aspergillosis is rare and represents the breakdown of a high degree of natural resistance to a fungus widely disseminated throughout nature. Every gradation of intensity may occur from that of a mild bronchitis to that of rapidly necrotizing caseous pneumonia depending upon the interplay of the pathogenetic factors. In the presence of the allergic diathesis bronchial asthma may be caused by this fungus. The occurrence of aspergillosis together with pulmonary tuberculosis may have especial significance. In a case of the "superficial" type herein described iodides proved of benefit.

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ACRODYNIA

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[From the Pediatric Service of Dr. Bela Schick]

This case is being reported because of its comparative rarity in urban centers and because of the methods used in its study.

History (Adm. 399041). H. H., a six year old boy, was admitted to The Mount Sinai Hospital on September 29, 1936 with a history of pain in the hands and feet, profuse perspiration, itching of the skin, weakness and irritability, of six months' duration.

The family history was irrelevant. Birth and development were normal. At the age of thirteen months he had had an attack of dysentery, following which redness of the hands and feet developed, associated with profuse perspiration and itching of the trunk. This persisted for about one year and was described by the mother as being similar to the present illness. The boy had never been outside of New York City. There was no history of pica and his food was, in general, the same as that of the rest of the family.

Six months prior to admission he contracted pneumonia and bilateral otitis media for which a double mastoidectomy was done. Convalescence was protracted. Three months later he developed a morbilliform rash which was diagnosed as measles. The presence of Koplik's spots was not known. For three weeks thereafter he had severe pains in all the digits, associated with a reddish cyanosis of the hands and feet. Intense itching caused almost continuous scratching of the skin and gnawing of the fingers. Perspiration was so drenching as to wet the bedclothes. A month after the appearance of the rash, blisters appeared on the palms of the hands; these ruptures and desquamation of the epithelium followed. In addition, he had sleep inversion. These symptoms continued with slight improvement. Three weeks prior to admission a tonsillectomy was done.

Examination. The patient was a fairly well nourished boy who was not acutely ill. His expression was unhappy and tearful. The skin was constantly wet and was pigmented over the abdomen and sacrum, sites of the most intense scratching. When not scratching himself he usually gnawed at his fingers, but not to the extent of causing trauma. There was no loss of hair or teeth. The edge of the spleen was palpable and there was slight enlargement of the cervical lymph nodes. There was a soft systolic murmur at the apex. The blood pressure varied between 106 to 130 systolic and 60 to 82 diastolic. There was a persistent tachycardia, the

rate ranging from 120 to 140. The neurological examination was negative. The impression was acrodynia probably in the process of recovery.

Laboratory Data. X-ray examinations of the chest and long bones were negative. The blood chemistry, blood counts and urinalysis were normal. The Wassermann and Kahn tests were negative. The Mantoux test was positive with 0.1 mg. Traces of arsenic were present in the hair, nails and urine but within normal limits; this was true also of lead in the urine. The basal metabolic rate was high. Taken on two occasions it was plus 56 per cent and plus 50 per cent according to the Pirquet standard. (Sitting height, 61 cm. Weight, 20 kilos. Total calories for twenty-four hours, 1166 and 1123 calories.)

Course. During hospitalization, the itching became less distressing and the sweating lessened. The color of the hands and feet became a normal pink. Sleep inversion, however, continued up to the time of discharge. He was given a general diet and no special therapy.

Readmission. He was admitted about a year later for further study. At this time the pigmentation and excessive moisture of the skin were still present and the hands and feet were again a dusky red color. Itching was less evident and sleep inversion no longer present. The blood pressure was slightly elevated.

Treatment with acetylcholine by iontophoresis was begun. He was given 0.025 gm. acetylcholine in distilled water applied to the right hand every other day for seven treatments, with the current varying from 20 to 30 milliamperes; the duration of each treatment was from fifteen to twenty-five minutes. No improvement was observed (1, 2).

METHODS OF STUDY

The failure to find any etiologic factor in this case led us to study its mechanism. Examination of the capillaries by Dr. Sidney Leader showed them to be normal. Krogh has reported capillary dilatation in acrodynia.

Numerous records of the skin temperatures of the extremities, abdomen and head were taken following the method of Lewis (3). The results were all normal and indicate that, despite the chronic dilatation of the small vessels of the extremities, the ability to react to the stimuli of heat and cold was retained.

This normal reactivity of the vegetative nervous system was further demonstrated by results obtained following the administration of sympatho- and parasympatho-mimetic drugs. Epinephrine and histamine gave the usual reactions. Eserine sulphate, however, caused definite increase in the itching and sweating. Atropine produced no effect.

The method of Lewis for estimating the contractile strength of the capillaries was also tried out. A drop of adrenalin, 1 to 1,000, was placed on a normal part of the forearm, above the area of cyanosis. Back pressure was made by the blood pressure cuff. At this site the blanching per-

sisted up to a pressure of 108 mm. of mercury, the child's systolic pressure. This reaction is within normal limits (4). The same test was made in a cyanotic area. A back pressure of only 70 to 80 was necessary to overcome capillary contraction. This difference in contractile strength is to be expected from the cyanosis and indicates that the capillaries of the cyanotic extremities must be different from those elsewhere.

DISCUSSION

Clinically the case is typical of aerodynia. The onset with a morbilliform rash, the itching and excessive perspiration, the desquamation of the skin, the red cyanosis of the hands and feet and the hypertension are all characteristic.

The etiology appears to be as varied as the symptomatology. Particular care was taken in the history to determine whether there was excessive ingestion of rye bread, or whether there was any food idiosyncrasy to suggest poisoning by fungi, heavy metals or other toxins. Cases have been reported in which lead and arsenic seem definitely to be causative agents (5, 6). In such instances these metals were found in pathological amounts in the urine and/or in the hair. Cornsmut was apparently the etiologic factor in a group of cases reported in Zagreb (7, 8). (Cornsmut is a fungus whose pharmacology resembles that of ergot.)

The rarity of the disease in large cities is worthy of further mention. Only one other case has been admitted to The Mount Sinai Hospital in the past ten years and at Bellevue in the past eight years there have been only two cases from New York City on the pediatric wards. Yet practitioners in small communities meet the condition fairly often, occasionally in infants entirely breast fed. It is usually found that if the patients are hospitalized before they become seriously ill, recovery ensues, and occasionally recurrence follows removal to their former environment.

The interpretation of the striking difference in incidence between urban and rural centers is difficult. It is likely that in the latter areas, children are exposed to etiological agents which are not present consistently in large cities. Recovery on removal from the former environment would bear this out. Sporadic cases like our patient, on the other hand, may be due to primary defect or weakness of the vegetative nervous system in which a spontaneous disturbance of function occurs. This would account for the fact that in this case improvement in the hospital was only slight.

Considering the various factors which may produce the symptoms of aerodynia—arsenic, lead, cornsmut and those cases in which no cause was found, it seems evident that aerodynia is a syndrome of varied etiology and not a disease entity.

Our findings in this case conform to those reported by Feer (9): "If we wish to avoid outraging the facts (or circumstances) we must assume in our cases a neurosis of the entire vegetative nervous system. It remains

unclear whether individual phenomena are related to a disturbance of the sympathetic or parasympathetic apparatus. Our efforts to obtain better insight by means of pharmacological investigations have led to no success."

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THE TAKATA-ARA REACTION IN VARIOUS DISEASES IN CHILDHOOD¹

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The Takata-Ara test was first proposed in 1925 by Takata as a sero-diagnostic procedure to differentiate bronchopneumonia from lobar pneumonia. He reported that the test was positive in the latter, an observation which was never confirmed.

In 1929 Jezler (1) first used the test in hepatic disease. He concluded that the test was positive in cirrhosis of the liver in both the blood serum and ascitic fluid. He also obtained positive reactions in cases of acute yellow atrophy of the liver. Since Jezler's work a voluminous foreign literature on this subject has accumulated. The test was first reported in the American literature by Crane (2) in 1934. He simplified the technique and pointed out the value of the test in differentiating cirrhosis of the liver, in which it was positive, from carcinoma of the liver, in which it was usually negative. Several subsequent reports have appeared, including an excellent brief summary by Kirk (3).

Technique. The technique described by Crane, which was used in this work is as follows: To the first of a series of seven small tubes, each of which contains one cubic centimeter of physiological saline solution, the serum to be investigated is added. The serum must be from non-hemolysed blood. Progressive dilutions are made adding one cubic centimeter to the first tube and transferring one cubic centimeter of the mixture to the next tube in succession. Dilutions of 1:2 to 1:128 are obtained. To each tube 0.25 c.c. of 10 per cent sodium carbonate and 0.3 c.c. of the Takata reagent are added. The reagent is made by mixing equal volumes of 0.5 per cent mercuric chloride and 0.025 per cent basic fuchsin; it must be prepared freshly for each test. The result is positive if a flocculant precipitate appears in the fourth to the seventh tube after twenty-four hours. Observations are usually made at thirty minutes, two hours and twenty-four hours. The degree of "positiveness" is dependent on the amount and rapidity of appearance of the precipitate.

The mechanism underlying this test is, as yet, not entirely understood. A colloidal solution of mercury-oxy-chloride in blood serum is formed by the mixture of the reagents and the serum. The stability of this colloidal suspension determines the reaction. There are many factors which affect

¹ Read before the pediatric section of the New York Academy of Medicine, April 15, 1936.

the stability of such a complex colloid—the pH, the free ions of the blood, especially the ammonia ions, the surface tension, the serum proteins and both the total amounts and the ratio of albumin to globulin. The amount of fibrinogen is also a factor, and the qualitative differences in these proteins is perhaps as important as their quantitative relations.

It has been quite definitely shown that albumin is the protective agent in this colloidal suspension, while the globulins are the precipitating or antagonistic substances. All investigators agree that the total amount of globulin in the serum is most important. A negative Takata-Ara can be converted to a positive one by adding sufficient globulin to the serum. A few investigators have emphasized the ratio of albumin to globulin as most important. D'Antona and Pellegrini (4) stress the presence of certain euglobulin and pseudo-globulin fractions in positive sera. Only Magath (5 and 6) emphasizes fibrinogen. Oefelein (7) has shown that the addition of ammonia ions causes flocculation. The pH is important experimentally. The addition of free acid, especially the lower fatty acids, causes precipitation. The addition of free base causes a positive reaction to become negative. However, the pH is not very important clinically, since it varies so little even in severe disease. Kirk reports an excellent series of parallel blood protein and Takata-Ara determinations. He finds that 95 per cent of sera containing over 3 per cent of globulins give positive reactions. Only 8 per cent of sera with globulin less than 3 per cent give positive results. His average figures for negative tests compare favorably with the normal blood protein figures—albumin 3.91, globulin 2.18. Thus he concluded that the Takata-Ara reaction is not diagnostic of cirrhosis of the liver or of any other morbid process. The test is likely to be positive in any disease in which the globulin level is elevated. That the test is not entirely dependent on the quantitative levels of the blood proteins is shown by the infrequency of positive reactions in chronic nephritis, in which the protein levels are very much changed. This has been explained in the following manner. In severe hepatic cirrhosis a large amount of blood from the intestinal circulation is shunted past the portal circulation and the liver by various anastomotic venous channels. This may cause certain qualitative changes in the albumin and globulin fraction of the serum in hepatic disease which lead to positive tests. In chronic nephritis, on the other hand, the excretion of albumin causes a quantitative rather than qualitative change in the blood proteins.

About two thousand eight hundred Takata-Ara tests have so far been reported in the literature. In three hundred and seventy-five cases of cirrhosis of the liver three hundred and fifteen, or 85 per cent, were positive. The test was negative in 97 per cent of cases showing no hepatic disease. Aside from cirrhosis of the liver, positive tests have been reported in acute yellow atrophy. Only occasional positives are mentioned in

catarrhal jaundice. Positives are also reported in acute and chronic nephritis, advanced tuberculosis and extreme cachexia. In healthy individuals the test is always negative.

There are only two studies reported in children. Paschedag and Püschel (8) demonstrated a very large number of mild positives in the third to

TABLE 1
Summary of results obtained with the Takata-Ara reaction

CONDITION	CASES POSITIVE	CASES NEGATIVE
Infectious hepatitis (catarrhal jaundice).....	4*	7
Phosphorus poisoning.....	1*	—
Absence of biliary system in newborn.....	1†	—
Icterus of six weeks' duration in newborn.....	—	1
Macrocytic anemia in newborn.....	—	1‡
Chronic cardiac decompensation.....	1	3
Chronic nephritis with edema.....	4	—
Persistent unexplained lipemia.....	1	—
Severe anemia, rickets, and hepatosplenomegaly in an infant.....	1	—
Still's disease with amyloidosis.....	—	1
Lipoid nephrosis.....	—	1
Hepatosplenomegaly, unclassified.....	—	3
Diabetes with hepatomegaly.....	—	1
Diabetic ketosis.....	—	2
Von Gierke's disease.....	—	2
Celiac disease.....	—	3
Sickle-cell anemia.....	—	1
Hemolytic anemia.....	—	1
Allergic conditions—urticaria, eczema, asthma, serum disease, nirvanol reaction.....	—	11
Chronic diffuse tuberculosis with hepatosplenomegaly...	1	—
Subacute bacterial endocarditis.....	1	—
Lupus erythematosus.....	1	—
Infectious diseases—pneumonia, rheumatic fever, pyuria, otitis, sepsis, undulant fever.....	—	10
Sarcoma of rib.....	—	1
Kaposi's disease.....	—	1
Chronic lymphadenitis, unclassified.....	—	1

* Became negative on recovery.

† Was negative at onset of illness.

‡ Post mortem examination showed severe degeneration of liver parenchyma.

sixth week of scarlet fever. This is evidence of toxic damage to the liver which, as is known, may occur in scarlet fever at this time. A few of these cases also had renal damage during this period. Recht (9) studied the Takata-Ara test in nurslings and young children. He used a modified technique and interpretation and, therefore, his results are not comparable to ours or to those obtained in any of the studies in adults.

Relation to other Tests. The Takata-Ara test has little relation to other liver function tests. It does not parallel either the icteric index, Van den Bergh, bilirubin tolerance, galactose tolerance, cholesterol partition, or the dye excretion tests. The liver function, with which it is concerned, is believed to be associated with protein metabolism, as the liver is considered to be the regulator of the blood protein levels.

Observations. Over one hundred determinations were made since 1934. The cases studied (see table 1) were principally instances of liver dysfunction. Several allergic children and a number who were suffering from some infection or metabolic disturbance were studied.

Of eleven cases of catarrhal jaundice or, as it is now better known, acute infectious hepatitis, four cases showed positive reactions at some time during the course of the disease. In two of these children the Takata-Ara was positive for more than two months. Both had had severe icterus for over three months. In all of the eleven cases the reaction was negative at the time of discharge. Several of these children were seen at the Follow-Up Clinic and their reactions still were found to be negative.

In one case of phosphorus poisoning the Takata-Ara was positive for six weeks and then became negative. In this instance the Takata-Ara was positive after all other tests of liver function were normal. At this time the child appeared to be entirely well symptomatically, but the liver remained slightly enlarged.

In an infant with complete absence of the biliary system, the test was negative at the time of an exploratory laparotomy, when the surgeon reported well marked liver cirrhosis. Three weeks later the Takata-Ara was positive. At this time the child was well on a down-hill course with severe cholemia.

In a premature infant who had macrocytic anemia of an obscure etiology the Takata-Ara was negative. Post mortem examination, however, revealed severe parenchymatous degeneration of the liver.

CONCLUSIONS

The Takata-Ara test appears to be a rather coarse index of the efficiency of one of the many liver functions. It is positive only late in cirrhosis of the liver, as is well shown in the case of complete absence of the biliary system. It is also positive in some cases of infectious hepatitis, most likely in those in which the liver damage is considerable. Positive results are obtained in some cases of nephritis and in severe chronic infectious diseases with cachexia.

A positive result indicates severe damage to the liver. With recovery of the hepatic function the test may become negative again. It is also obvious that a negative test in a case of hepatic disease is of little significance.

The application of this test as a diagnostic measure in pediatrics is limited, being helpful mainly in the analysis of cases showing hepatic disease.

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ACUTE SUPPURATIVE PERICARDITIS COMPLICATING SEPTICEMIA

REPORT OF A CASE WITH RECOVERY AFTER OPERATION*

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Although acute suppurative pericarditis is not so rare a disease as had formerly been believed, its incidence and mortality are still such as to warrant the report of any new occurrence, particularly in the event of a recovery. With this objective, as well as to illustrate several interesting features of sepsis, the following case is presented.

Sixteen months ago, a seven year old boy fell and sustained an abrasion over his right knee. The lesion promptly healed. Three days later, sudden generalized aches and pains, associated with chills and fever, developed. This was followed, in two days, by an acute inflammatory process in the left shoulder. This localized anteriorly and was drained at another institution. The abscess was subperiosteal, in the upper end of the left humerus, and, on culture, yielded staphylococcus aureus.

Subsequently, the clinical picture of sepsis continued, several blood cultures revealing staphylococcus aureus. Repeated transfusions and staphylococcus antitoxin were administered without apparent effect. Metastatic foci soon invaded the left mandible, lungs, and soft parts of the right arm. Ten days after the onset, evidences of cardiac embarrassment supervened, and, on the eighteenth day after onset, clinical and X-ray evidences of pericardial effusion were noted, which, in view of the uncontrollable sepsis with suppurative metastasis to various structures, led the patient's physician to the belief that a suppurative pericarditis existed.

The child was almost moribund when, twenty-one days after onset, the patient came under Dr. Neuhof's observation. A pericardial tap was positive for pus. Under local anesthesia (which, because of the patient's condition, was hardly necessary), the pericardial sac was opened through an interior subcostal approach. Ten ounces of thick pus under great tension escaped. Both visceral and parietal pericardial layers were covered by a thick, grayish exudate. A culture of the fluid grew out staphylococcus aureus. In view of the child's extremely poor condition, only a brief emergency procedure was carried out.

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The clinical response to this procedure was immediate. The general condition, relieved of the cardiac tamponade, rapidly improved. The septic factor, however, still appeared to be in a state of activity during the next few weeks. A low grade fever persisted, while blood cultures remained positive and multiple new abscesses, involving soft tissues and bone, formed in various places. Locally, despite the profuse drainage of thick pus, the pericardial wound tended to close.

Accordingly, the child was transferred to this hospital and a revision was performed five weeks after the primary pericardiostomy. General improvement had so progressed that this time avertin and gas-oxygen anesthesia could be administered and a more thorough surgical procedure achieved. A wide opening of the pericardial sac was made followed by the evacuation of one to two ounces of thick yellow pus and the entry into many pockets of purulent exudate both behind and in front of the heart. The masses of thick, shaggy exudate were bluntly removed, exposing necrotic visceral and parietal pericardial layers. The operative procedure was concluded by approximating the edges of the pericardial wound to the edges of the neighboring soft tissue wound.

Thereafter, slow but progressive improvement, both locally and generally, occurred. The thick, profuse and purulent pericardial drainage gradually became scanty and thin, while both pericardial layers began to resolve. Five weeks after the revision, the discharge from the pericardium completely subsided and the wound was permitted to close. Interval X-ray examinations and clinical signs, disclosed the pericardial enlargement to be receding. Fever slowly but steadily subsided, yet additional metastatic abscesses continued to appear. A particularly large one formed subfascially on the inner aspect of the upper third of the left thigh; it rapidly healed following drainage.

The child was up and about and, seven weeks after admission (or fifteen weeks after onset), was discharged from the hospital in good general condition, with a granulating closed pericardial wound, and with no cardiac abnormalities. At that time the pericardial problem was solved, but the metastatic foci required further attention.

Five months later, upon readmission for sequestrectomy of the left humerus, the boy was observed to be in good health, gaining weight, and with a completely healed pericardial wound. During the next six months, however, it rapidly became apparent that the septic factor had not been entirely eradicated; several abscesses developed in various parts of the body, most of them related to bone, accompanied by a progressive anemia. About one month ago, that is, fifteen months after the onset of the sepsis, the child was readmitted for drainage of a large lumber abscess. His general condition was good, but anemia was pronounced. A blood transfusion was accordingly administered. A blood culture at this time was negative.

In view of the fact that one of the very early abscesses in the left mid-thigh (the one previously referred to in this presentation) had opened recently after having been healed for many months, this zone was regarded as a possible site from which the continuing metastatic foci were derived. Accordingly, this wound was explored, a sequestrum was removed from the soft parts, and the tract was followed and found to reach into the depths of Hunter's canal. Here, the femoral vein was found to be thickened, partly collapsed, and was regarded as a possible viaduct for the foci distributed in various parts of the body. Accordingly, this portion of the vein was excised. It was reported as the seat of a periphlebitis.

No metastatic foci have appeared since this operation, but it was too recently performed to determine as yet whether or not it has solved the problem.

In conclusion, several features should be emphasized. Technically, this case illustrates a two stage pericardiostomy. Clinically, it illustrates a severe clinical picture of sepsis, dominated, for a brief period, by a more severe picture of suppurative pericarditis which subsided after adequate surgical drainage, leaving the scene to a persistent sepsis. The pericardial element, therefore, was only an incident in the general pattern.

DISCUSSION

DR. HAROLD NEUHOF: Any case of suppurative pericarditis in which operative recovery occurs, is of course of interest, but in my opinion operative recovery is more concerned with the type of pericardial infection than with the operative technic that is employed. Early diagnosis probably also plays some rôle in the question of recovery. The former factor, however, is more important. Given a case such as this, in which the general septic infection took care of itself, so to speak, or required nothing more than drainage of various metastatic abscesses, the outlook for cure by correct surgical management of the suppurative pericarditis proved to be good. I have had experience with other cases, however, in which the septic state continued, to lead to a fatal issue, despite successful drainage of the infected pericardial sac. There are two instances which I can recall in which the pericardial sac was found at autopsy to have been adequately drained and yet the patients died of their underlying infections.

Concerning the recognition of the existence of suppurative pericarditis, it cannot be too strongly stressed that there should be no hesitation in exploratory puncture of the pericardial sac if suppurative pericarditis is suspected. It is perhaps not sufficiently realized that the roentgenological features of the pericardial effusion are only evident when a considerable accumulation of fluid exists. In a recent case, clinical evidences of suppurative pericarditis were clearly present at a time when the roentgenologic features were equivocal and when exploratory puncture should have been performed. Aspiration was not carried out until a much later stage

at which time not only was the roentgen film positive, but the pericardial sac was tense with an enormous amount of pus. In the case under discussion the family physician was insistent on the diagnosis of suppurative pericarditis before the roentgen film was characteristic of pericardial effusion. Because of the latter fact, those who saw the child in consultation were unwilling to perform the diagnostic tap, which he believed was indicated on clinical grounds.

Concerning the technic of operation in the above reported case, the only feature of interest is the two stage operation. The child's condition at the time of the first stage was so bad that any procedure other than an emergency release of tension by simple evacuation would probably have been fatal. The pathology, as noted at the second operation, at which time the process had reached a subacute state, is therefore of considerable interest, and its surgical management involved wide exposure of all surfaces of the heart.

INFLUENZAL PNEUMONITIS

CASE REPORT

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The following report is made to emphasize the prevalence of a pneumonitis which is not recognized unless routine roentgen examinations are made in cases of influenza with minor respiratory symptoms (1, 2, 3). The similarity in roentgen appearance to that usually seen in pneumoconiosis is also discussed.

Acute influenzal pneumonitis may be confused roentgenologically with pulmonary processes, such as acute bronchitis, bronchiectasis, bronchopneumonia, pulmonary abscess, tuberculosis, lymphangitic carcinoma and, as in this case, with pneumoconiosis. In any case of influenza with even apparently insignificant pulmonary symptoms a roentgenogram will ordinarily show the presence of an exudative process in the lung (1, 2). Bronchopneumonia not of influenzal origin usually produces more definite signs and more severe symptoms than the involvement of the lungs, shown by the roentgenogram, would suggest. The rapid absorption, which is characteristic of influenzal pneumonitis, is not seen in bronchiectasis, pulmonary abscess, tuberculosis, carcinoma or pneumoconiosis.

History (Adm. 400758). A 40 year old Italian male was admitted to the hospital on November 7, 1936. He gave a history of malaria in youth and exposure to poison gas during the World War. He had been engaged in dusty occupations, including cement work, for many years but had been unemployed for the three years prior to admission. During the War he developed a chronic cough which was productive of one-half cup of yellowish-white sputum daily. This sputum was never foul or bad-tasting. Two years before admission there had been on a few occasions a slight streaking of the sputum with blood. He was well until five days before admission when he began to feel weak, noted increased cough and blood-streaked sputum. During the next three days he felt feverish with chilly sensations but was not confined to bed. At no time did he complain of dyspnea or pain in the chest. The productive cough continued and he sweated profusely at night. The throat felt raw and hoarseness developed with temporary loss of the voice. During the two days before admission he coughed up large amounts of sputum mixed with dark red blood. There was no loss of weight.

Examination. On admission the patient appeared to be acutely ill;

his temperature was 101°F. There was hoarseness and the larynx showed a slight ulceration of the left vocal cord, which disappeared one week after admission. Examination of the heart was negative. Numerous sonorous, sibilant and occasional, moist râles were heard throughout both lungs, but otherwise the lungs were negative. A firm spleen was palpable one finger's breadth below the left costal margin. A slight conjunctival icterus was noted. There was no clubbing of the fingers. The remainder of the physical examination was negative.

Laboratory Data. Hemoglobin was 54 per cent; white blood cells 8,400; red blood cells 4,030,000; reticulocytes 9 per cent; platelets 330,000; icteric index 6; sedimentation time 20 minutes. Repeated sputum examinations were negative. Bronchoscopic examination was negative.

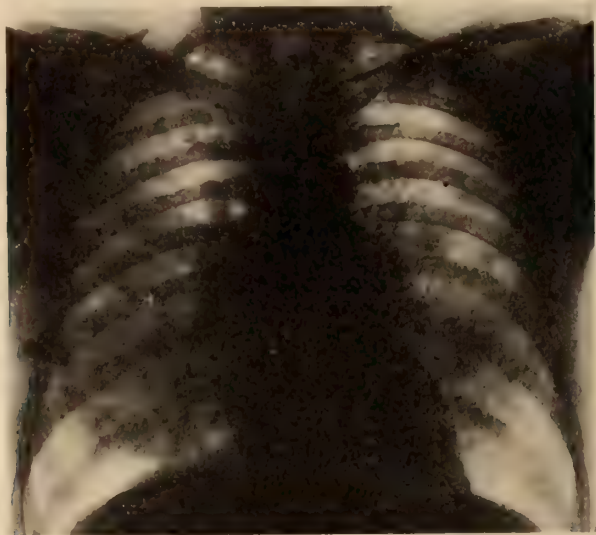


FIG. 1. Roentgen examination of the chest on admission showing confluent peribronchial infiltrations.

Roentgen Examination. On admission the roentgen examination (Fig. 1) showed confluent peribronchial infiltrations extending from the roots of both lungs into the pulmonary fields. On the right side these infiltrations extended to the lateral chest wall. There was a compensatory emphysema at the bases of both lower lobes and the upper portions of both upper lobes.

One week after admission the roentgen examination showed a disappearance of the infiltrations, except for an irregularly localized area in the left lower lobe. Within this area there were areas of increased aeration about one-half centimeter in diameter (Fig. 2).

Two weeks after admission the roentgen examination showed a complete

disappearance of all the infiltrations with no abnormality apparent in the lungs (Fig. 3).



FIG. 2. Roentgen examination of the chest one week after admission showing complete disappearance of pulmonary infiltrations except for an irregular area in the left lower lobe which contains areas of rarefaction.

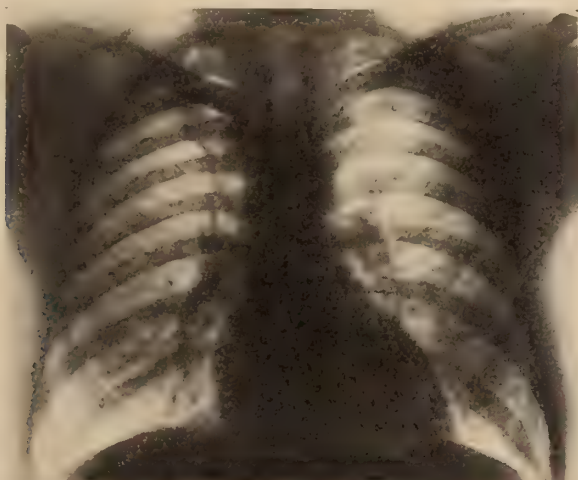


FIG. 3. Roentgen examination of the chest two weeks after admission showing complete resolution.

Course. With bed rest and symptomatic therapy the bloody sputum and cough decreased markedly and the temperature fell to normal. The patient was discharged three weeks after admission with no evidence of disease.

An incidental finding was a congenital hemolytic icterus, as evidenced by the slight conjunctival icterus, elevated icteric index, secondary microcytic anemia, high reticulocyte count, splenomegaly and a history of intermittent asymptomatic icterus since childhood. Three of his five children were examined with negative results.

Comment

Since the roentgen appearance of the lungs in this patient, who presented the clinical picture of an acute infection and had a history of long exposure to dusts, was similar to that usually seen in pneumoconiosis, it was important to determine whether the lung picture was due to pneumoconiosis or to influenzal pneumonitis. This differentiation was made by a series of films showing rapid resolution of the pulmonary process, thus eliminating the consideration of pneumoconiosis in which the pathologic changes are persistent.

Influenzal pneumonitis is characterized by an inflammatory process occurring largely about the bronchi and the peribronchial blood vessels and in the septa of the lung (4). In pneumoconiosis there is enlargement and partial fibrosis of the lymphoid deposits along the course of the peribronchial lymph vessels with thickening of these vessels and stasis of their contents (5). The anatomical configurations produced by these two processes cast similar roentgen shadows.

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EARLY FUSION OF ELBOW EPIPHYSES

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[From the Orthopedic Service]

The advent of roentgenology has made possible great accuracy in the studies of the centers of ossification. Normal variations in the time of appearance and fusion of the epiphyses are dependent on race, climate and heredity. Attention has been called to the difference in ossification in the male and female skeleton and that development of the female is advanced over that of the male of the same age (Pryor). It is also recognized that endocrine disorders cause changes in skeletal growth with characteristic variations in the time of appearance and fusion of the epiphyses (Clark, Engelbach and McMahon, Shelton, etc.). The stage of epiphyseal development is considered a more reliable index of endocrine and metabolic status than other means of examination in children.

The average time for fusion of the centers at the elbow joint is given as ranging from 15 to 18 years of age (Hodges, Cohn, etc.). The following case was considered of interest because of complete fusion of the epiphyses at the elbow joint in a girl of $12\frac{1}{2}$ without any evidence of endocrine disturbance or other etiology.

CASE REPORT

History (Adm. 415078). M. B., a female, $12\frac{1}{2}$ years of age, entered the hospital following a fall in which she sustained a fracture of the medial epicondyle of the left elbow. The X-ray examination of the elbow joints (Fig. 1) showed complete fusion of the epiphyses, including the conjoined epiphysis at the distal end of the humerus, and those at the proximal end of the radius and ulna. Roentgenograms of the knees, wrists and shoulder (Fig. 2), showed these epiphyses to be ununited. The past history was that of a normal full term infant, breast-fed for six months and fed by a formula for six months. Childhood diseases included pneumonia complicated by empyema, measles and chicken pox. The menses had started at the age of $11\frac{1}{2}$.

Examination. The patient was a well nourished and well developed adolescent female, 62 inches tall and weighing 123 pounds. The physical examination was entirely normal except for the fracture at the elbow and such minor physical defects as adolescent acne and dental caries. Blood studies were normal. The final impression was that of a normal adolescent female of $12\frac{1}{2}$, presenting complete union of the epiphyses at



FIG. 1. Elbows showing epiphyses united



FIG. 2. Wrist and knee showing epiphyses ununited

the elbow without any evidence of growth disturbance or endocrine dysfunction.

COMMENT

The case indicates that the epiphyses at the elbow may be fused as early as 12½ years of age in an otherwise normal female. It serves as a reminder of the fact that use of the time of fusion of the epiphyses as a guide to age or the presence of endocrinopathy must be done with full appreciation of the wide variations that may normally occur, and that these variations are more marked than is indicated by the tables representing the average normal.

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Isadore Goldstein

December 9, 1879-December 23, 1937

Dr. Isadore Goldstein was born in New York City fifty-eight years ago. He was graduated from Cornell University Medical School in 1904 and served on the staff of The Mount Sinai Hospital from 1904 to 1905. While on the house staff he acquitted himself creditably and was outstanding for his keen observation. He then entered general practice and did clinical work in pediatrics, gynecology and otorhinolaryngology. While working in otolaryngology he appreciated the importance of ophthalmoscopy in complicated cases. At that time it was practically impossible to obtain courses in ophthalmology in this country. It was his good fortune to come under the influence of Dr. Alexander Duane who not only gave him his first instruction in ophthalmology but directed and supervised his training. Later he became associated with Drs. John E. Weeks, Arnold Knapp, John M. Wheeler and Bernard Samuels -all great teachers - who helped him in his career. He also spent several summers in post-graduate work in Vienna. Whenever knowledge was imparted to him he absorbed it and always retained it.

He was associated with the New York Eye and Ear Infirmary for twenty-four years and was on the attending staff of The Mount Sinai Hospital for the last thirteen years. For many years he taught operative surgery. To instruct the younger men was his chief aim, and all associated with him profited. He possessed the particular faculty for pioneer work in surgery and some of his operative technique and procedures were original. The department of ophthalmic pathology at The Mount Sinai Hospital was established by him and he will long be remembered for this.

His contributions to ophthalmic literature were prolific and varied. He wrote particularly on pathology of the eye and plastic surgery.

Outstanding was his capacity for work and in the operating room his endurance was remarkable. His confidence and pleasure in his work was an inspiration to all associated with him. The younger men who received training under him have benefited by his wisdom, his excellent technique and his natural desire to impart knowledge.

His life was one of achievement and he made a notable record. To have worked with him was a rare privilege; I hope his students will emulate him and carry on.

KAUFMAN SCHLIVEK.

ABSTRACTS

AUTHORS' ABSTRACTS OF PAPERS PUBLISHED ELSEWHERE BY MEMBERS OF THE
MOUNT SINAI HOSPITAL STAFF

Members of the hospital staff and the out-patient department of The Mount Sinai Hospital are invited to submit for publication in this column brief abstracts of their articles appearing in other journals.

Streptococcus Haemolyticus Bacteremia. G. SHWARTZMAN and J. L. GOLDMAN.
Arch. Surg. 34: 82, January 1937.

This report presents an analysis of one hundred and sixty-eight cases of streptococcus haemolyticus bacteremia in which positive blood cultures were obtained. These cases were grouped according to the route of invasion into the blood stream and studied in relation to age, seasonal incidence, prognosis and the clinical picture observed.

The following classification was formulated: (A) *Streptococcus haemolyticus* bacteremia following peripheral infections, erysipelas, infections of the upper respiratory tract, thrombosis of the lateral sinus, acute otitis media with meningitis, pulmonary infections, osseous and articular infections, surgical infections and gynecological infections. (B) *Streptococcus haemolyticus* bacteremia associated with leukemia, agranulocytic angina, neoplasms, diabetes, rheumatic cardiovascular disease, tuberculosis and unknown causes. In this group no direct relationship could be established between the associated disease and the bacteremia.

Certain phases of the blood culture technic were largely responsible, it was believed, for the high incidence of positive blood cultures for streptococcus haemolyticus, especially when limited to fluid mediums. The features of particular value were the large quantity of blood drawn, the variety and enrichment of mediums employed, the careful adjustment of pH of the mediums, the daily subcultures, spreads and prolonged observation.

Analysis of the blood cultures revealed that the number of organisms cultivated from the blood stream, especially in fluid mediums, had diagnostic and prognostic significance, and that there was a close correlation between the bacterial picture and the clinical picture observed. The diagnostic import of these blood cultures was demonstrated by the fact that in the groups in which the mortality was relatively low a high percentage of the blood cultures was positive in fluid mediums only, while in the groups with a relatively high mortality there was a high percentage of positive blood cultures in both solid and fluid mediums. The occurrence of a positive blood culture with the technic employed always indicated a general infection (septicemia) clinically. The data embodied in this report disclosed that the finding of streptococcus haemolyticus in the blood stream on one occasion, even in extremely small numbers, was of important clinical significance for diagnosis, prognosis and indication for surgical intervention.

The Etiology and Therapy of Ulcerative Colitis. A. WINKELSTEIN. *Am. J. Dig. Dis. & Nutrition* 3: 839, January 1937.

Ulcerative colitis is now a common disease, characterized by a chronic, recurrent course. Its clinical and pathologic features do not distinguish it from the specific colitides. Etiologically, it does not seem to be an entity. A few cases are unrecognized amoebic colitis. A larger percentage (perhaps 20 per cent) are chronic bacillary dysentery. The etiology in the remaining majority is unknown. The more important therapeutic measures are: (1) azochloramid rectal instillations, (2) repeated blood transfusions, (3) routine anti-amoebic therapy (emetine and carbarsone), (4) in proved cases of bacillary dysentery, massive doses of anti-dysentery serum, (5) in the cases of unknown etiology, antitoxic *B. coli* horse serum (good results are reported with this form of therapy), (6) in the chronic, recurrent cases, active immunization with *B. coli* vaccine and toxin in the interval stages.

Ileostomy seems to be the best surgical procedure. Partial colectomy is occasionally indicated. Using these therapeutic measures, there is apparently a decreased mortality and an improved clinical course in many cases.

Choline-Esterase Activity of Human Sera, with Special Reference to Hyperthyroidism.

W. ANTOPOL, L. TUCHMAN AND A. SCHIFRIN. *Proc. Soc. Exp. Biol. & Med.* 36: 46, February 1937.

The acetylcholine esterase activity of the blood serum was determined in five hundred individuals, including normal and pathological cases. A modification of the Ammon gasometric method was utilized. The acetylcholine esterase was relatively high in cases of untreated hyperthyroidism. It is suggested that such activity may be one of the elements related to the so-called sympathicotonicity or vagotonicity of an individual. Many of the sera obtained from patients with jaundice, cirrhosis of the liver, hepatitis, anemia, arthritis, active rheumatic fever, and hyperpyrexia reveal pronouncedly depressed values.

Eruption Resembling Lichen Scrofulosorum Coincident with Non-Tuberculous Pulmonary Disease. E. T. BERNSTEIN. *Arch. Dermat. & Syph.* 35: 255, February 1937.

In an unusual example of lichen pilaris seu spinulosus, the eruption resembled lichen scrofulosorum in many particulars, as attested by the acceptance of the latter diagnosis by many competent dermatologists. The coincidence of the dermatoses with pulmonary disease appeared to corroborate the diagnosis of lichen scrofulosorum, of tuberculous etiology.

However, careful investigation revealed that the pulmonary process was not tuberculous from the clinical, surgical and laboratory points of view, and two biopsies of numerous sections of skin, disclosed non-specific histologic alterations unlike those encountered in characteristic lichen scrofulosorum.

When adequate histologic study fails to reveal characteristic changes, conditions reported as lichen scrofulosorum should be subjected to close scrutiny. In this manner, errors in diagnosis will be avoided in many cases.

A Radiographic Device for the Anteroposterior Mensuration of the Ethmoids and Sphenoids. S. FINEMAN. *Radiology*, 28: 2, 238, February 1937.

Accurate measurement of the depth of the posterior nasal sinuses is important in certain cases. A simple apparatus is described and illustrated which enables the roentgenologist or rhinologist to measure directly, on the roentgenogram, the depth of the posterior sinuses. The apparatus consists of a lead ruler notched in centimeters, which is fastened in the mid-sagittal plane of the skull. Regardless of the technique used in making the sinus roentgenogram, the magnification of the ruler and skull structures is always the same. The distance between any two points on the skull can be read off, therefore, directly on the ruler.

Myringitis Bullosa Hemorrhagica. S. KARELITZ. Am. J. Dis. Child. 53: 2, 510, February 1937.

A clinical study of myringitis bullosa hemorrhagica was made. One hundred and forty-five ears affected by this condition were observed. Analysis of the cases as to sex, age, season of occurrence and relation to the presence or absence of tonsils and type of disease which it complicated, was made. The results indicated that this is a mild, most likely external myringitis which resolves spontaneously in about 90 per cent of the cases, and that it should not be regarded as its dreaded facsimile, formerly associated with influenza. The frequency of occurrence of myringitis bullosa hemorrhagica caused me to suggest the possibility that this type of infection has become more common in recent years.

Placental Fluid in Measles Prophylaxis. S. KARELITZ, M.D., C. K. GREENWALD AND A. J. KLEIN. J. Ped. 10: 2, 170, February 1937.

Experimental evidence is presented which indicates that placental fluid has the same measles prophylactic value as that of equal quantities of immune adult serum. The results justify the deduction that placental fluid obtained from women immune to measles is equal to, and interchangeable with, immune adult serum in measles prophylaxis. Experimental evidence is given which proves that the diphtheria antitoxic titre of fluid expressed from human placentas and the corresponding blood serum obtained from the general circulation during the last stage of labor, are alike. This corroborates similar experiments previously recorded by authors.

Placental Immunity. A Method of Determining Dosage of Placental Globulin in Measles Prophylaxis. S. KARELITZ, M.D., C. K. GREENWALD AND A. J. KLEIN. J. Ped. 10: 2, 175, February 1937.

A method is described for measuring the dosage of the whole globulin extract of human placenta for measles prophylaxis. As corroborative evidence of the validity of this method, the results obtained in the treatment of one hundred and seventy-four children, susceptible to and exposed to measles, are recorded. The reactions to placental globulin are discussed and pertinent observations reported.

Persistence of Duodenal Ulcers After Suture of an Acute Perforation. R. LEWISOHN. Surg. Gynec. & Obst. 64: 172, February 1937.

Many patients have persistent ulcer symptoms after suture of an acute perforation. These symptoms are due to the fact that the anterior wall ulcer persists in spite of the previous perforation or that, in addition to the anterior ulcer which perforated acutely and was sewn over, a posterior wall ulcer existed which, of course, was not affected by the surgical procedure. The diagnosis must be made on clinical grounds, as the roentgen-ray examination will show distorted duodenal bulbs in all cases in which patients were subjected to a previous operation on the duodenum. If severe ulcer symptoms persist after the suture of a perforation has been done, patients should be reoperated upon and a partial gastrectomy should be carried out.

Status of Cholecystogastrostomy in Obstructive Jaundice due to Carcinoma of the Head of the Pancreas. G. D. OPPENHEIMER, A. GLASS AND F. NETTER. J. A. M. A. 108: 707, February 1937.

The purpose of this report of a study of thirty-four patients with obstructive jaundice who were treated by cholecystogastrostomy was to evaluate the results of biliary intestinal anastomosis. The percentage of error in operative diagnosis, as judged by subsequent findings, was 13.3. The mortality was 41.3 per cent. The average postoperative duration of life was seven months. An unusual case of carcinoma of the head of the pancreas (proved by autopsy) with death twenty-nine months

after the surgical procedure is mentioned. The problems of cholangitis following biliary intestinal anastomosis and stenosis of the stoma are discussed. Of seventeen patients who survived operation, ten were definitely benefited. The operation should be performed when there is a non-removable obstructive lesion of the common bile duct below the cystic duct.

Localization of Ventricular Extrasystoles in a Human Heart with Right Axis Deviation.

M. PRINZMETAL, B. S. OPPENHEIMER and S. DACK. J. A. M. A. 108: 620, February 1937.

Left ventricular extrasystoles were produced during a surgical operation by direct electrical stimulation of the left ventricle in a patient with constrictive pericarditis whose electrocardiogram showed right axis deviation. Following the operation right ventricular extrasystoles were induced by tapping the chest wall overlying the right ventricle.

The main ventricular deflection of left ventricular extrasystoles was upright in Lead I and that of right ventricular extrasystoles was inverted in Lead I. This does not conform to the newer terminology now widely used for the localization of extrasystoles and bundle-branch block. These observations suggest that the newer terminology can be safely applied only in the presence of a normal electrical axis or of left axis deviation.

Thrombo-Angiitis Obliterans and Addison's Disease in the Same Patient. S. SILBERT.

J. A. M. A. 108: 551, February 1937.

A case of thrombo-angiitis obliterans and Addison's disease occurring in the same patient is described. The report of the two diseases in one individual is unique in medical literature. The patient, aged 20 years, presented characteristic features of both ailments. He was treated with injections of hypertonic salt solution and adrenal cortical hormone. He made a striking recovery from both diseases and is at present in excellent condition. The possibility of the Addison's disease being due to thrombo-angiitis obliterans of the adrenal vessels is discussed and is considered improbable. Since thrombo-angiitis obliterans occurs in individuals who have a diminished thyroid-adrenal-gonad function the simultaneous occurrence of Addison's disease is not inconsistent. It was noted that the special preparation of cortical hormone used was much more efficacious than the commercial extract available.

Fractured Ribs with Paradoxical Motion. J. B. STENBUCK. J. A. M. A. 108: 470, February 1937.

Cases of fractured ribs are considered in the light of the abnormal physiological changes or complications that may occur, rather than as cases of broken bones. In fractured ribs, anatomical restoration and attention to function is almost never necessary. The most important complications are pneumothorax, hemothorax, and subcutaneous emphysema. The unique cases reported demonstrate a complication of paradoxical motion with apparent disturbance of the mediastinal vascular structures.

The Psychology of the Hymen. I. S. WILE. J. Nerv. & Mental Dis. 85: 2, 143, February 1937.

The history of the hymen involves the history of chastity and virginity in terms of masculine desire for primal physical possession. The psychological elements related to the hymen are due to the fact that, when intact, it was held to be an infallible sign of virginity. The presence of an intact hymen does not prove non-coitus any more than its absence attests defloration. Its psychological import has been founded

upon the conscious level and its relations to hysteria, neurosis and less severe mental disorders are bound up in human conflicts concerning the meaning of its presence, absence or mutilation. The psychology is woven from past economic interest, social taboo and religious ideology. Changing attitudes towards the hymen bear witness to current changes in human attitudes and sentiments.

Hepatic Excretion in Man of the Various Bile Acids Following Their Oral Administration. H. DOUBILET. *Proc. Soc. Exper. Biol. & Med.* 36: 50, March 1937.

Cholic and desoxycholic acids were fed in quantities of 10 to 15 grams daily to a patient with a complete common bile duct fistula. This patient was refed his own bile daily. It was found that after feeding cholic acid the concentration of both cholic and desoxycholic acids rose in the excreted bile. After feeding desoxycholic acid, the concentration of cholic acid fell, while that of desoxycholic acid rose. It was concluded therefore that cholic acid was much more effective than desoxycholic acid in raising the concentration and total output of bile salts in the excretion of hepatic bile.

Resistance of the Sphincter of Oddi in the Human. H. DOUBILET AND R. COLP. *Surg., Gynec. and Obst.* 64: 622, March 1937.

By means of a specially designed apparatus, the manometric resistance of the sphincter of Oddi to the flow of fluid was recorded directly on a kymograph in patients with T-tube intubation of the choledochus. It was shown that spasm of the sphincter of Oddi does occur in the human. The degree of spasm could be correlated with the appearance of the X-ray films after lipiodol visualization of the biliary tract. In addition, it was shown that in the absence of the gall-bladder, the sphincter did not relax after ingestion of a meal or the injection of olive oil into the duodenum. Magnesium sulphate by duodenal tube caused relaxation of the sphincter, while HCl caused spasm lasting ten minutes which could be prevented by atropinization. Both morphine and pantopon caused severe spasm lasting over three hours, which was not influenced by atropin. Papaverine and adrenalin had a negligible effect on the tone of the sphincter.

Significance of Blood Vessels in Human Heart Valves. L. GROSS. *Am. Heart J.* 13: 275, March 1937.

This report describes the findings in 100 non-vascularized normal human valves; 44 human hearts in which the valves were vascularized but appeared grossly normal; 13 hearts with extinct monovalvular rheumatic disease; 50 human hearts, 50 calf hearts and a number of rabbit and guinea pig hearts injected by Wearn's technic; uninjected calf, swine, rabbit and guinea pig hearts; and swine, ox and human embryos serially sectioned. It is shown that the so-called normal vascularized human hearts present widespread stigmas which in incidence and distribution bear striking resemblance to the findings in undisputed extinct rheumatic specimens. Reasons are given which indicate that rheumatic fever which has gone on to complete healing is responsible for the formation of these blood vessels. A description is given of the normally vascularized calf heart valves, and attention is drawn to the differences between these valves and their blood vessels, and those sometimes found in human hearts. It is further shown that, while ox and swine embryos display blood vessels in their valves, these are not found in the heart valves of human embryos. As a consequence, there exists no rational embryogenetic basis on which to explain the occurrence of blood vessels found in human hearts.

A discussion of injection technic together with new observations reinforces the belief that such technic affords no information on the problem under discussion

which cannot be better obtained by microscopic observations on serial sections. The conclusion is drawn that blood vessels do not exist in normal valves or must be very rare.

The So-Called Congenital Bicuspid Aortic Valve. L. GROSS. Arch. Path. 23: 3, 350, March 1937.

A study was made of sixteen hearts possessing the so-called congenital bicuspid aortic valve. These hearts presented no associated developmental abnormalities. Strategic cardiac sites and serial sections of the commissures were examined microscopically. In the majority of these there were stigmas which strongly implied an associated, generally extinct, rheumatic process. This was apart from the obvious secondary lesions (bacterial endocarditis, syphilis). Evidence is presented which supports the hypothesis that a degenerative process (Mönckeberg type) in a minority of instances, and a rheumatic process in a majority of instances, leads to the formation of the so-called congenital bicuspid aortic valve in the adult. The pathogenesis of the lesion on a rheumatic basis is described, and attention is drawn to the compatibility of this view with the predisposition of the valve with this deformity to subacute bacterial endocarditis. It is concluded that Osler's macroscopic criteria do not necessarily indicate a congenital lesion. It is suggested that the microscopic criteria of Lewis and Grant should be verified by study of a representative number of cases in which the bicuspid condition of the aortic valve is of indisputable congenital developmental origin.

Additional Data On The Treatment Of Uterine Bleeding With Snake Venom. M. A. GOLDBERGER AND S. M. PECK. Am. J. Obst. & Gynec. 33: 3, 469, March 1937.

Twenty functional uterine bleeding cases and five cases of uterine bleeding due to fibromyomas were treated. The method of administration of snake venom is presented in detail. In some cases, a hypersensitivity to snake venom protein occurred about the tenth day. Desensitization was accomplished by reducing subsequent injections. The control of uterine bleeding probably results from the action of the venom on the uterine capillaries, making these vessels more resistant to hemorrhage. A summary of the results show that seventeen of the twenty functional uterine bleeding cases responded favorably to moccasin venom therapy. One of the three cases reported as failures was studied over a period of four years. In this case, venom therapy was effectual for three years and ineffectual in the fourth year. The poor result was explained by the discovery of a one and one-half inch uterine polyp. Removal of polyp effected a complete cure. Uterine bleeding resulting from fibromyomas is not controllable by moccasin snake venom therapy.

Chemical Investigations on the Active Principles of the Phenomenon of Local Skin Reactivity to Bacterial Filtrates. I. Purification by Dialysis, and Attempts at Fractional Precipitation. G. SHWARTZMAN, S. MORELL AND H. SOBOTKA. J. Exper. Med. 65: 323, March 1937.

A quantitative biological assay of the products obtained from the dialysis of *B. typhosus*, *meningococcus*, and *B. coli* culture filtrates has been undertaken. It was found that the active principles of the phenomenon of local skin reactivity to bacterial filtrates were retained by cellophane membranes. An appreciable purification was thus effected, amounting, on the average, to about a threefold increase in reacting potency per milligram of dry weight and of nitrogen. Attempts to purify bacterial filtrates by the fractional precipitation of their concentrates with dilute alkali, acid, and alcohol were unsuccessful.

Pituitary Radiation for the Relief of Menopause Symptoms. S. H. GEIST AND M. MINTZ. *Am. J. Obst. & Gynec.* 33: 4, 643, April 1937.

A series of seventy-five patients suffering from menopausal symptoms was treated by radiation of the pituitary gland. There were twenty-five additional control cases. In 85 per cent of the cases sweating was markedly decreased and in 75 per cent of the cases there was a marked diminution in the frequency of flushes. Other symptoms, such as headaches, nervousness, dizziness and palpitation were all improved. The improvement in the symptoms lasted from two to six weeks. Repetition of treatment again resulted in amelioration of symptoms. The treatment is limited in its usefulness because only a restricted number of exposures can be given. The result of this therapeutic measure suggests a relationship between the pituitary gland and the menopausal syndrome.

Tumors of the Pelvic Girdle. E. M. BICK. *J. Bone & Joint Surg.* 13: 2, 402, April 1937.

Tumors of the pelvic girdle are not rare. Half of them are primary tumors, if one excludes cases in which pelvic involvement is merely the terminal phase of a generalized metastasis. They are most liable to present the clinical picture of an atypical sciatic or sacro-iliac syndrome, or that of "low-back pain." Motor disability of a non-specific character in an extremity during the course of a sciatic or sacro-iliac syndrome calls for a roentgenographic study of the pelvis even though previous roentgenograms have been negative. A consideration of pelvic girdle tumor must enter into every routine examination of the patient with "low-back", "sacro-iliac", or "sciatic" symptoms.

This distribution tends to confirm the observation that the sciatic or sacro-iliac syndrome may be due to any factor which disturbs the muscular mechanics about the gluteal or iliac region, and is not specifically related to affections of the sacro-iliac joint, the sciatic nerve, or any definite muscle.

Posterior Fossa Tumors without Papilledema. IRA COHEN. *J. Nerv. & Ment. Dis.* 85: 411, April 1937.

During a five and a half year period thirty-five posterior fossa tumors, other than intrapontine growths, were verified by operation or necropsy. Seventeen of these cases, nearly fifty per cent, enter the hospital without papilledema. The types of tumor represent a cross section of the usual lesions encountered both extra- and intra-cerebellar. In some, the history was of long standing. Neither the location of the lesion nor the time of morbidity explains the absence of fundus changes. Ventricular dilatation and elevated cerebrospinal fluid pressure were found in the majority of the cases. It is possible that an explanation may be found in the variations in the vascular pressure in the retinal vessels. While an understanding of the absence of papilledema is highly desirable, the practical lesson to be learned from this communication is that normal fundi are frequently seen in patients with posterior fossa tumors.

Twenty Years' Experience with the Citrate Method of Blood Transfusion. R. LEWISOHN. *Ann. Surg.* 105: 4, 602, April 1937.

Post-transfusion chills are due to foreign protein reactions and to defects in the distillation of the water. Careful cleansing of instruments, tubing and glassware, as described by Rosenthal, has reduced the incidence of chills following transfusion of citrated blood to about one per cent. In 1935, six hundred and fifty-three citrate transfusions by the gravity method were given on the wards of The Mount Sinai Hospital. Eight chills were observed in this series. The slow-drop transfusion can be utilized only when citrated blood is used. Drop infusion or transfusion is an important factor in the prevention of reactions.

Foreign Bodies in External Auditory Canal. H. ROSENWASSER. *Am. J. Surg.* 36: 1, 96, April 1937.

The factor of paramount importance in the removal of foreign bodies in the external auditory canal in children, is that all manipulations be performed under general anesthesia. Good illumination, preferably reflected light, is a necessity. No attempt should be made to remove any aural foreign body until one is prepared to cope with complications. Hydrosopic foreign bodies require removal at the earliest moment, but should be treated with absolute alcohol before any efforts at removal are undertaken. The method of choice in the removal of non-hydrosopic foreign bodies, is that of forceful syringing with warm water or solution of boric acid, provided there is no perforation in the tympanic membrane. Syringing having been tried repeatedly under general anesthesia or being contra-indicated, the physical properties of the foreign body will then determine whether one uses blunt curettes, blunt or sharp hooks, silver probes, forceps or whatever instruments are available. After removal of the foreign body, ammoniated mercury ointment 5 per cent should be applied liberally to the walls of the external auditory canal.

In the instances in which it becomes necessary to employ a post-auricular incision in order to remove an impacted foreign body, one must pack the external auditory canal firmly postoperatively to avoid atresia. If the middle ear is discharging, it is safer to risk an atresia by not packing, than it is to pack and court an otitic complication.

Absorption of Fat from the Ileum in Human Beings. H. DOUBILET AND M. REINER. *Arch. Int. Med.* 59: 5, 857, May 1937.

Experiments on fat absorption were carried out on a patient who had accidentally acquired a temporary Thiry fistula of the middle portion of the ileum. In this case the ileum was found to secrete a fluid containing about 2 per cent lipids. Bile acids were found to increase the secretion of fluid without increasing the concentration of lipids in it. Desoxycholic acid caused a greater outpouring of fluid than cholic acid. Emulsions of olive oil and of oleic acid were absorbed from the ileum even in the absence of bile acids. In small amounts bile acids were found to have little effect on the rate of absorption of fats, but in large amounts they increased the volume of secretion and so tended to reduce the rate of absorption of fat.

ANNOUNCEMENT

Through the kindness of Mrs. Charles Klingenstein and Dr. Alfred Meyer, provision has been made whereby graduating interns and a limited number of members of the Out-Patient Department may be placed on the mailing list of the *Journal of The Mount Sinai Hospital* for a period of one year, on payment of fifty cents (to cover the mailing expenses).

Those who are interested may apply to Dr. J. H. Globus, Editor-in-Chief of the *Journal*.

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JOURNAL
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THE LIFE HISTORY OF FASCIOLA HEPATICA*

JUAN BACIGALUPO

[Professor of Parasitology, Medical School, University of Buenos Aires, S.A.]

The importance given in the past few years to the investigation of patients for the presence of ova or parasites everywhere has shown that many diseases considered to be endemic in certain countries or specific regions are, in fact, much more prevalent and extended outside of their natural environment, to such an extent that they can no longer be called tropical diseases, but, in a broader sense, parasitic diseases.

On the other hand, and as the result of the departure from this old routine, parasitologists have demonstrated that some parasites, as in the case of *Fasciola hepatica*, believed to be a laboratory curiosity, are much more common, this fact being proved recently by the discovery of large numbers of human cases of hepatic distomiasis. Hence, in Argentina only one case had been discovered up to 1914 as the result of a post mortem examination performed on the body of an Arabian who died of an infectious disease of unknown etiology, but from whose liver twenty-five adult parasites were removed. After this event, the routine examination of stools and bile by transduodenal drainage has brought to light the presence of seven more cases. In Cuba, and particularly in Havana, the presence of twenty-six cases was discovered by means of the routine examinations of the stools and bile. This has happened in other countries and in my book on this disease, published in the year 1934, I was able to report, after an exhaustive study of medical literature up to that time, 130 cases of hepatic distomiasis which at the present time run into the hundreds.

Our methodical investigation was started in the year 1927 when, in association with Drs. Bengolea and Velazco Suarez, we discovered our first human case of hepatic distomiasis produced by *Fasciola hepatica*. A short time later, in the year 1930, another case from the same region was found and was carefully studied by us from the clinical standpoint. The fact that both patients had eaten watercress, a perennial herb, as salad induced me to visit the region in order to study the intermediate host. After

* Lecture delivered at The Mount Sinai Hospital, February 15, 1938.

a careful investigation of the snails found there, I came to the conclusion that *Limnæa viatrix d'orb* was the specific intermediate host in Argentine and probably in all South America.

Fasciola hepatica (Fig. 1) is a flat parasite whose habitat is the gall bladder and biliary ducts of man and, in particular, of domestic animals which live nearby,—namely, cattle, sheep and so forth. It is leaf-shaped and hence its name. In hundreds of specimens taken from animals the size was established as follows:

	millimeters
Length, maximum	14 to 31
Length, average.....	26 to 30
Width, maximum.....	7 to 15
Width, average.....	8 to 10

Its shape is not absolutely regular, as in the anterior extremity; there is a triangular process called *cephalic cone*. On the ventral surface there are two suckers—one at the extremity of the cephalic cone and the other, or acetabulum, at its base. These are organs of attachment and locomotion, the anterior being the beginning of the digestive tube. This digestive system is incomplete, as it has an excretory pore on the dorsum of the parasite almost at its posterior border.

Fasciola hepatica is hermaphroditic. The genital pore is median, half way between the oral and ventral suckers and through it the eggs are passed into the biliary ducts and in the bile to the intestines. Hence their presence in the feces.

These eggs are large, ovoid and operculated and of a light yellowish brown color due to bile pigment. They measure 135 to 150 microns in length by 65 to 90 microns in breadth in man and 115 to 145 microns in length by 70 to 90 in breadth in experimental animals. In natural infestation in animals their size is 108 to 145 microns in length by 65 to 90 in breadth. The characteristic feature is the presence of an operculum in one of the extremities, easily seen in the field of the microscope. Through this operculum the embryo or miracidium escapes.

This egg can be mistaken in feces with the egg of the fish tape-worm or *botriocephalus latus*, but the latter is smaller in size measuring only from 60 to 70 microns.

Now we shall study the life history of this parasite from the egg to maturity in the adult stage.

The fresh egg contains in its interior an ovular cell and a small amount of nutrient material. In water a ciliated embryo is developed and different factors hasten or retard this process, among which factors temperature is the most important. At a temperature of 10 to 12°C. the miracidium reaches maturity and hatches in eighteen to twenty-five days. Seasons play an important rôle in this development; in summer at the above mentioned temperatures the embryo is fully developed in eight or ten days and

escapes from the egg in twelve, fifteen or twenty days. Light also is an important factor; under the same conditions, plus light, the whole process is hastened two, three or more days.

When the egg is mature, a miracidium appears in its interior. This miracidium is only a ciliated embryo which is clearly seen through the transparent egg membrane (Fig. 2). At this time this embryo moves



FIG. 1

actively and two characteristic features stand out prominently, namely, a cephalic spine and a black spot known as the ocular spot. This spot has the shape of an X and is formed by two crescents—when the miracidium is mature it raises the operculum and through the opening it escapes from the egg in fifteen to twenty seconds, according to the pictures shown (Fig. 3).

After its emergence the miracidium is very active running in all directions across the visual field and looking for its natural intermediate host,

Limnaea viatrix, dying within a short time later, if no snails are in the vicinity.

In this stage the miracidium is long with a spine in its anterior extremity and measures in fixed preparations in hot Bouin medium from 113 to 130 microns in length by 29 to 40 microns in breadth with cilia, except at the



FIG. 2



FIG. 3

level of the anterior spine. The X-shaped ocular spot is formed by two pigmented cells with their convexity towards the inner aspect. This embryo also presents an excretory apparatus and, according to some authors (Thomas), the remains of a digestive system. Now the miracidium lives in water under favorable conditions about twenty-four hours. Its

span of life should really be from four to five hours, within which period of time for further development it must find its natural host, which in South America is represented by a snail of the genus *Limnaea*, *Limnaea viatrix* d'orb.

From the very first moment the investigator is amused, as it were, by the biological phenomenon called "miracidial attraction"—namely—if free miracidia and snails of different species, including *Limnaea viatrix*, are placed in water in a Petri dish, these miracidia are only attracted by the latter species whose integument they penetrate. The other species are not touched.

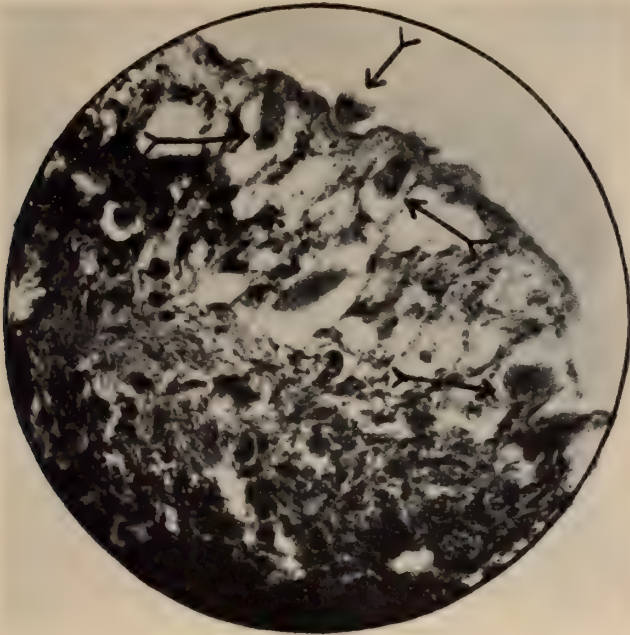


FIG. 4

The miracidium enters the soft tissues of the snail with the aid of its anterior spine and slowly, in from thirty minutes to two hours, the active penetration of the mollusk is completed (Fig. 4). The first thing we observe is the disappearance of the cilia and the splitting of the ocular spot. Now it works its way through the tissues into the lungs and, once in this organ, it begins to increase in size without losing its shape. Round cellular masses, the future rediae, which later acquire an elongated shape, appear. This original miracidium, through metamorphosis, is now converted into a sporocyst which, consisting of a wall without a digestive tube, contains these rediae in its interior. In fifteen days the rediae pierce the wall of the sporocyst and migrate into the hepatopancreas through the tissues

(Fig. 5). They are long, measuring from 230 to 250 microns and have an oral opening, a pharynx and an esophagus. In the anterior extremity they also have a sharply outlined ring, an opening through which the cercariae escape and in the posterior extremity two processes corresponding to the remains of the organs of locomotion. The interior of the redia at this stage contains cellular masses.

In the hepatopancreas the cellular masses of the redia undergo segmentation and are transformed into cercariae. Each redia produces twenty-two or twenty-four cercariae. These cercariae leave the redia through the opening mentioned above and, piercing the tissues of the snail, emerge from the integument and swim about in the water.

The shape of the cercaria is characteristic. The anterior portion is more or less elongated and ovoid and measures from 260 to 300 microns by

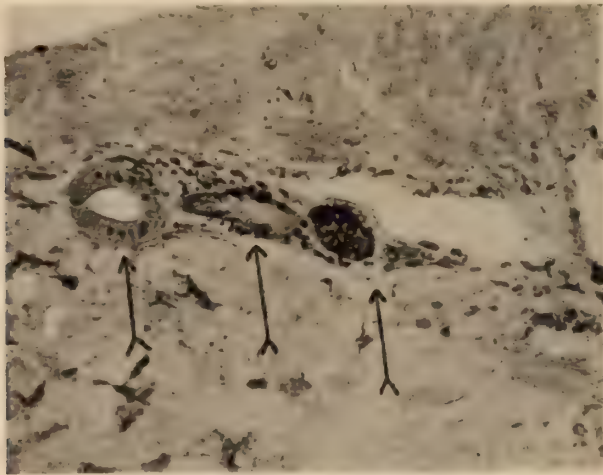


FIG. 5

225 to 240 in its lesser diameter. It has a tail which acts as the organ of locomotion in water (Fig. 6). The cercaria has two suckers: one ventral in the center and the other oval in the anterior extremity opposite the tail. From the oral sucker, one tube and bulb, the pharyngeal bulb, extends backwards to the posterior sucker and there it divides into two lateral tubes which end in a blind extremity. All this is the digestive apparatus of the cercaria. There are also large numbers of cytogenic cells for the final process of encystment.

The life of the cercaria, as such, is very short, not over twenty or thirty minutes. After this lapse of time motion becomes very sluggish and it settles down to discharging its tail, as minute white spherules, on aquatic vegetation, objects, or just free in the water. At this moment the cercaria is an encysted cercaria or infective metacercaria, spherical in shape, viable

and inactive, but potentially ready to be transformed into an adult *Fasciola hepatica* upon ingestion by man or mammals. The cycle of development in the snail is, according to our observations, from fifty-seven to sixty days.

In some species of limnaea studied the development of daughter rediae in summer and cercariae in winter has been observed. In *Limnaea viatrix* this development was not observed and only in one case were daughter rediae found in winter.

All our investigations were made with snails collected in their natural habitat and then born and developed in our laboratory.

We studied the geographical distribution of *Fasciola hepatica* in cattle, as well as the geographical distribution of *Limnaea viatrix*, and we found always a biological relationship which plays a highly important rôle in



FIG. 6

the prevalence of parasitic diseases in certain regions and countries of the world. We also found, in Buenos Aires, infected *Limnaea viatrix*, which discovery proves that the mechanism of infection, as observed by us in the laboratory, takes place also in nature.

Let us consider now the mechanism of infestation of man and mammals and how the parasite reaches its natural habitat, namely, the bile ducts.

We have made our investigations with laboratory animals, as they acquire the experimental infection very readily.

The infection is transmitted through vegetables, and sometimes water, which contain the infective metacercariae or encysted cercariae. The most common vegetable which grows in water is watercress and our two patients gave a history of having eaten watercress from the same source.

In the duodenum the metacercariae excyst and the small distoma, now free, pierces the wall of the intestine and reaches the peritoneum on the

way to the liver through an unknown selective affinity for this organ. In twenty-four hours all the parasites lie on the capsule of the liver. We have fed experimental animals with material containing a known number of metacercariae and, within the same period of time, we have recovered each one of them from the surface of the liver.



FIG. 7

The first lesion to be noticed in the liver is the appearance of white spots consisting of fibrinoid necrosis (Fig. 7) through which the young fasciola enter the organ in order to reach the biliary ducts where they grow to maturity. It is our belief that these degenerative lesions of the liver are produced by a toxin excreted by the parasite in order to prepare the tis-

sues for its penetration, as otherwise they would perish in the visceral peritoneum.

As to the erratic fasciolas, as observed in the case of a student of medicine in Argentine, it must be accepted as an erratic young distoma which migrated to the bladder, an unusual habitat. The parasite reaches maturity in the biliary ducts and in this location it begins to extrude eggs into the intestines through the bile within a period of from fifty-four to ninety days after the initial ingestion of the metacercariae.

SUMMARY

1. *Limnaea viatrix* d'orb is the intermediate host of *Fasciola hepatica* in Argentine and probably in South America.
2. This mollusk may be infested throughout life both in the young and adult stages.
3. In our experience we have never observed the development of daughter rediae in summer and only once in winter.
4. The development of the parasite in the snail takes from fifty-seven to sixty days.
5. The cercariae live from twelve to thirty minutes.
6. The journey of the young cercariae to the liver is through the peritoneum
7. The eggs appear in the stool from fifty-four to ninety days after the ingestion of the metacercariae.
8. *Limnaea viatrix* has been found infested in nature, which fact proves its rôle in the transmission of the disease.
9. There is a close relationship between *Fasciola hepatica* and *Limnaea viatrix* in regard to the prevalence of hepatic distomiasis.

DIAGNOSIS

This is made from the recovery of eggs of *Fasciola hepatica* from the stools. Our first two cases were discovered in this way, but there is a source of error which must be considered.

The ingestion of infested liver as a food, as well as liver and bile for therapeutic purposes, may at times be mistaken for an actual infection. I have seen two patients whose stools contained eggs of *Fasciola hepatica*, notwithstanding the fact that they were not suffering from hepatic distomiasis. Upon examining commercial specimens of bile, I found that some of them contained eggs and these were ingested and passed without undergoing any change. With experimental animals and insects I proved that helminth eggs may pass through the digestive tract without being affected in any way. This discovery does not invalidate the use of liver or bile for food or therapeutic purposes, as the eggs do not develop without the link of the intermediate host. In order to be more accurate in the diagnosis of hepatic distomiasis, it is necessary to verify the presence of eggs

in the bile obtained by transduodenal drainage. Serological reactions have no significance and are devoid of any practical value.

The prophylaxis of hepatic distomiasis must be in harmony with the life history of the parasite. In the first place, vegetables and water from infested regions should be discarded and the water, if used at all, should be properly treated beforehand.

Before closing, I must say a few words in regard to treatment. Until recently this parasitosis was indifferent to all sorts of treatment. In our patients we demonstrated beyond doubt the specific and rapid action of emetin in hepatic distomiasis. Four years later they were found to be perfectly well and with no signs or symptoms of the disease. Recently many patients have been successfully treated in my country, and even here in this hospital and in Cuba, where Professor Kouri and his associates have taken care of fifteen patients with 100 per cent cures.

RECURRENT EPITHELIOMA OF ARM

METHOD OF COVERING DEFECT AFTER RADICAL EXCISION ILLUSTRATING TWO USEFUL TYPES OF SKIN TRANSPLANTATION

JOHN H. GARLOCK, M.D.

[From the First Surgical Service]

In the surgical treatment of cutaneous malignancies, the surgeon is frequently confronted with the problem of covering large defects at the time of the original operation. Numerous methods are available to take care of such a situation, but a happy outcome becomes dependent solely upon the proper choice of procedure and the form of skin transplantation adopted. Experience has shown that the surgical defect created by the excision of a cutaneous malignancy is most adequately cared for by the use of a pedicled skin flap which includes skin and subcutaneous fat. This type of skin transplantation has much to commend it by reason of the fact that there is a greater chance for a complete "take," provided the surgeon is cognizant of, and makes use of, the primary principles of plastic surgery concerning adequate blood supply, lines of the skin, the estimation of the length of the flap as compared with the width, the obliteration of dead spaces, etc.

In certain situations one may make use of a free full-thickness skin graft. With all the factors making for success of this type of skin transplantation remaining operative, the surgeon can expect a positive "take" in 90 to 95 per cent of the cases. A third form of skin transplantation is available in the split-thickness skin graft which is in between a Thiersch graft and a full-thickness graft. With the application of proper technique the surgeon may expect almost 100 per cent "take."

Conditions often arise when it becomes necessary to make use of two or more types of skin transplantation in order to cover surgical defects. A knowledge of the principles involved and the methods available will curtail the number of operations required and thereby shorten considerably the patient's convalescence. The following case is an example of the use of two forms of skin transplantation at one sitting to take care of defects created by the surgeon after excision of a cutaneous malignancy.

CASE REPORT

History (H. H. Adm. 274103). The patient, a woman of 55 years, was first seen at the New York Hospital on July 5, 1927, at which time she presented a large epithelioma in the left antecubital fossa which had de-

veloped during the preceding three years in the scar of an extensive burn sustained during childhood. This tumor was quite large, measuring about



FIG. 1. Photograph of arm when patient was first seen in July, 1927. Note the extensive scarred area following the old burn and a large squamous cell epithelioma in the antecubital fossa.



FIG. 2. Result obtained following wide excision of the epithelioma, and the application of a pedicled skin flap from the lateral chest wall. Photograph taken one year after operation.

two and a half inches in diameter, and presented a fungating bleeding surface. It was excised widely and the defect thus created was covered by a skin flap from the lateral chest wall which had been previously pre-

pared as a tubular flap. This was done in stages. Healing occurred without incident, and the final result may be noted in figure 2. She remained well until January 1934, when she noted the beginning of a small recurrence at the inner edge of the skin flap just above the elbow joint. This gradually increased in size until, upon admission to The Mount Sinai Hospital on July 9, 1934, it measured an inch and a half in diameter. There were no palpable regional lymph nodes. Operation was undertaken on July 13, 1934 at which time the neoplastic ulcer was excised with a wide margin

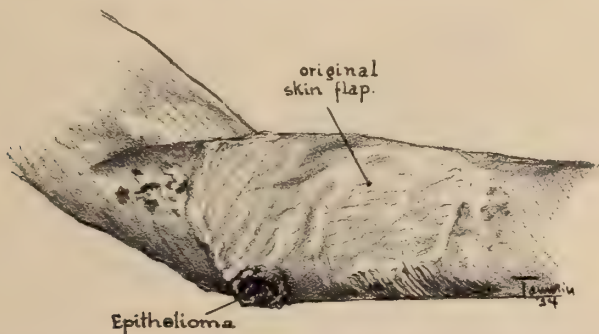


FIG. 3. Appearance of arm on admission to The Mount Sinai Hospital in July, 1934.

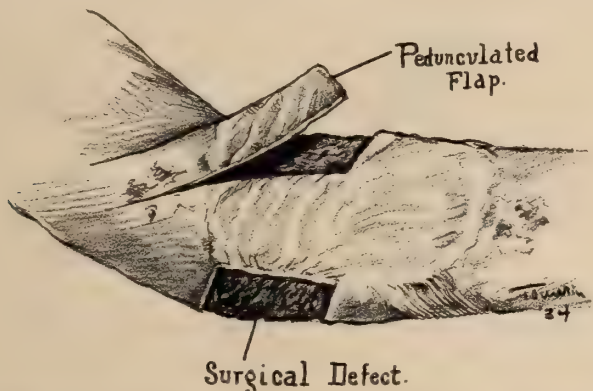


FIG. 4. Defect created by excision of epithelioma with a wide margin of skin. Elevation of pedunculated skin flap from the outer side of the lower arm and elbow.

of surrounding normal skin and subcutaneous fat. This left a defect about two and a half inches square. The accompanying diagrams indicate the method used to cover this wound. A flap was raised from the outer aspect of the arm so that its length was no more than three times its width. The flap was then transposed and placed into the defect without kinking of its pedicle. The donor site of the flap could not be repaired by plastic undermining of the skin edges. This defect was then covered by a split-thick-

ness skin graft taken from the left thigh and sewn into place with a basting stitch of horsehair. The entire area was then covered with four thicknesses of gauze impregnated with three per cent xeroform ointment and a rubber sponge dressing applied to the split-thickness graft. Of necessity, in order to maintain proper pressure over the sponge, considerable pressure was also applied to the region of the skin flap. Convalescence was uneventful. The split-thickness graft "took" throughout its entire extent.

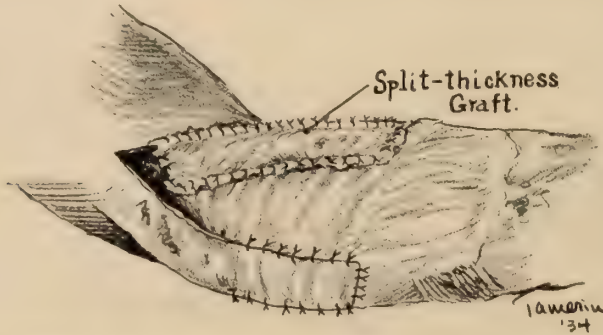


FIG. 5. The skin flap has been sewed into the defect and the donor site of the skin flap covered by a split-thickness skin graft taken from the thigh and sewed into place with a basting stitch.



FIG. 6. The pedicle of the skin flap has been divided transversely and its proximal part returned to its original site. The remaining wound at the elbow has been repaired.

The skin flap presented a small area of superficial necrosis at its midpoint. This was interpreted as being due to a turn of the bandage in the application of the original dressing. Eighteen days later the pedicle of the flap was divided transversely, and the two resulting wounds repaired with a few interrupted sutures of horsehair. The final result is indicated in figure 6.

To date, there has been no evidence of recurrence of the epithelioma.

DIVERTICULUM OF THE ESOPHAGUS

EXCISION IN ONE STAGE, AND SATISFACTORY RESULT

GABRIEL SELEY, M.D.

[From the Surgical Service of Dr. Harold Neuhof]

Diverticula of the esophagus were probably known for many years but it was Ludlow, in 1746, who was the first to observe and describe a case of pulsion diverticulum of the esophagus. In 1840 Carl Rokitansky divided the esophageal diverticula into pulsion and traction diverticula. The pharyngo-esophageal type are pulsion diverticula and are under discussion in this paper. Killian and Keith believe that the diverticulum arises between two definite parts of the inferior constrictor muscle, from the posterior wall of the pharynx in the median line at the level of the cricoid cartilage just above the pharyngo-esophageal junction. There is a weakness in the muscular wall below the last transverse fibers of the constrictor pharyngeus inferior and the lower circular and oblique fibers of the constrictor pharyngeus inferior muscle. Thus "pharyngeal" pulsion diverticulum would be the correct terminology. There are also reports of congenital pharyngeal diverticula arising from bronchial clefts in the vicinity of the tonsil or pyriform sinus. Moynihan described a hernia of the mucosa and submucosa through the muscular wall, which he believed to be another type. Lahey states that all sacs are in the midline or to the left so that incisions should be made on the left routinely. In the discussion of this point Sturgeon stated that he found seven out of twenty-two sacs on the right.

The treatment is either palliative or operative. If the patient is old and a poor risk, either gastrostomy should be done or, with the use of a thread as a guide, a sound should be passed to dilate the opening into the esophagus and overcome the spasm of the crico-pharyngeus muscle. Care should be taken to empty the sac after meals and before sleep, because if the sac is permitted to become too distended with fluid during sleep, cough and even asphyxiation may be produced.

If operative treatment is decided upon, operation should be performed promptly because a huge diverticulum leaves a large aperture at its neck where it opens into the esophagus and the dissection becomes very difficult. Operative treatment consists in extirpation of the sac, with or without previous gastrostomy. This latter procedure is usually reserved for those cases where it is impossible to feed the patient by mouth, even with the use of a tube or catheter passed into the stomach. It also must be men-

tioned that the passage of such a tube is often difficult, if not impossible, to accomplish.

Years ago various types of operative procedures were advocated, during which extirpation was not performed. However, with these methods recurrences were common and fistula formation very annoying. Girard in 1896 envaginated the whole sac into the esophagus, inserting two to three purse-string sutures during the process. In 1907 Goldman advised merely ligation of the sac to cause a necrosis. In the same year Gehle reported a cure by the following method: He removed the mucosa of the sac with a sharp spoon, introduced a stomach tube through it twisting the sac 180 degrees and tied it to the tube with a purse-string suture which also included the skin; six days later he removed the tube. Liebl, in 1910, suggested placing the diverticulum in the upper outer part of the wound and suturing it to the skin. Several years later Schmid conceived the idea of laying the sac out flat in the upper part of the wound and fastening it to the pharynx muscle.

The one-stage diverticulectomy. The discussion of the technique employed in a one-stage diverticulectomy, as well as of those steps common to the one- and two-stage procedures, is not based on the method devised by one man, but represents a summary of various types of procedures reported in the literature. The *anesthesia* is varied and includes local, nerve block, avertin and inhalation anesthetics of various sorts. The *incision* is either longitudinal along the anterior border of the sternocleidomastoid muscle, or transverse above the clavicle. The former incision extends from the hyoid bone to the clavicle and is the one most often employed. During the dissection the omo-hyoid muscle may be divided. The middle thyroid vein, inferior thyroid artery, and occasionally even the superior thyroid artery may require ligation. It is always advisable to visualize carefully the recurrent laryngeal nerve and, if necessary, to retract it mesially. The presence of a goitre may necessitate its removal and occasionally the sternal head of the sternocleidomastoid muscle may have to be severed for better exposure. After the sac has been completely freed, an esophageal bougie may be passed. Jackson and Shallow advise passing an esophagoscope and leaving it in place during the diverticulectomy. The *Gaub-Jackson maneuver* consists of passing an esophagoscope into the sac, illuminating it, and bringing it into the wound. An esophagoscope may also be used for emptying the sac. Small sacs may be ablated after a transfixion suture has been placed through the neck. Torek recommends incising the sac wall rather than the esophagus. The usual case requires a careful closure of the opening in the esophageal wall. Lahey employed ligation of the neck of the sac in four cases with carbolization of the stump and drainage. All these cases developed deep abscesses of the neck. Most authors suggest the use of drainage material consisting of either a rubber dam or a cigarette

drain. The latter is used especially in cases where the fundus of the sac dips down into the mediastinum.

Charles Mayo and Judd in 1910 advocated a two-stage diverticulectomy. At the first operation the sac was dissected out and attached to the sternocleidomastoid and anterior muscles. Ten to twelve days later the wound was reopened, a purse-string suture was placed around the neck of the sac, the diverticulum was then ablated and the sutures tied. In 1933 Lahey presented a series of thirty-five cases of pulsion diverticulum treated by two-stage operation without a death. He does not employ the one-stage procedure because of fear of a leak between the pretracheal and prevertebral fascia resulting in mediastinitis. By attaching the dome of the sac to the outer border of the sternohyoid muscle he brings the dome higher than the pharyngo-esophageal opening, allowing the sac to empty and the patient to swallow. During the second stage he advocates excision of most of the mucosa of the neck of the sac and packing of the remainder with boric ointment gauze to permit granulation and cicatrization of the wound. Lahey and others advocate the passage of bougies with the use of a guide every two to three months for one year.

The following two cases illustrate the management of two patients with huge esophageal diverticula treated by preliminary gastrostomy and one-stage diverticulectomy.

CASE REPORTS

Case 1. History (Adm. 391982). This 58 year old male presented himself in April, 1936. His family history was irrelevant and his past history included excessive use of alcohol, gonorrhea, and, at the age of 27, chancre, which was treated by mercury pills given orally for two years. No Wassermann test was done and no injection therapy instituted. His chief complaint dated back about eight years, when he began to experience difficulty in swallowing; this increased markedly in the six weeks before admission. Although he was able to swallow an entire meal with difficulty, he soon regurgitated it, and in spite of a ravenous appetite, he lost ninety-five pounds in four years; most of this was lost in the last six weeks, during which time hoarseness became a prominent symptom. Palpitation, dyspnea, and orthopnea were recent symptoms.

Examination. There was marked loss of weight; he weighed 102 pounds. The eyeballs were prominent. The heart showed a totally irregular rhythm; the blood pressure was 108 systolic and 80 diastolic. There was no evidence of visceral or central nervous system syphilis. The urine was negative; the blood urea nitrogen 51 mg. per cent; the sugar 90 mg. per cent; the chlorides 540 mg. per cent; the cholesterol 280 mg. per cent; the calcium 11.4 mg. per cent. The blood Wassermann tests were negative on two occasions. The basal metabolic rate was plus three per

cent. X-ray examination of the chest showed a collection of fluid and air in the superior mediastinum. Further examination with the use of barium by mouth revealed a large pocket anterior to the esophagus, measuring about three inches in diameter. No barium could be forced into the lower half of the esophagus, despite the various positions in which the patient was placed.

Course. Six days after admission, a Kader gastrostomy was performed for feeding purposes, since it was found impossible to pass a Levin tube into the stomach. Two days after operation, lavage of the diverticulum was

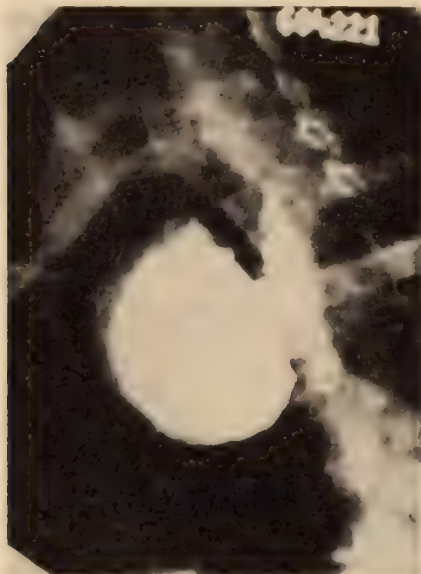


FIG. 1



FIG. 2

FIG. 1. (Case 1.) Preoperative film taken after ingestion of barium mixture, showing the huge diverticulum arising from the esophagus.

FIG. 2. (Case 1.) Postoperative film with use of contrast medium, showing a small residual pocket with the normal esophagus outlined below.

instituted. A Levin tube was passed into the diverticulum and it was irrigated with water until the return was fairly clear. This was continued daily up until the time of diverticulectomy. At first the return was foul and cloudy, but after several weeks became odorless and clear. During this period, the patient gained ten pounds in weight. One month after admission, the second operation was performed.

Operation. Under avertin gas-oxygen anesthesia a diverticulectomy for diverticulum of the esophagus was performed. A left-sided incision was decided upon because the patient stated that he made compression chiefly on the left side at the root of the neck when he wished to empty the diverticulum. An incision was made in front of the sternomastoid, partially

traversing the muscle with lateral retraction of the muscle together with the great vessels. The sheath of the vessels was not opened. The ribbon muscles were severed. The anterior belly of omohyoid was divided between clamps. The enormously dilated veins from the inferior pole and midlateral portion of the thyroid gland were severed between the ligatures. The left thyroid lobe was then drawn forward and retracted together with the trachea. There now presented a layer of tissue which was severed between forceps in order to isolate the region of the esophagus. An anemic membrane was then lifted out and gradually dissected out of the wound and was found to be the wall of the diverticulum. The latter was found to dip deeper and deeper into the mediastinum so that, when dissected free from the inflammatory tissue it was about four to five inches in each diameter. The space remaining in the mediastinum after full dissection was the prevertebral region down to the fourth or fifth dorsal vertebral body. The site of the neck of the diverticulum was the left lateral or lateroposterior aspect of the cervical esophagus directly opposite the thyroid gland. Relatively little of the diverticulum extended above this site, practically all of it being found in the mediastinum.

An attempt to outline the esophagus by passing a bougie failed. The diverticulum was ablated after the mediastinum had been packed off and what appeared to be a very large neck presented. This did not seem to be a satisfactory dissection of the neck and, accordingly, the passage of an esophagoscope was awaited. This at first only entered the region of the diverticulum and could not go past it. However, by making pressure in the wound against the end of the esophagoscope, the latter could be guided downwards to pass into a narrowed field. The esophagoscopist reported that he could not get beyond this narrowed field. With the esophagoscope in place the true neck of the diverticulum could be dissected out and proved to be about one and a half inches in each diameter. Ablation of the remains of the diverticulum was then carried out so that there would be a small excess. A two layer closure inverted the opening and an additional external layer appeared to adequately shut off the enfolded portion. A small excess pouch remained after this procedure. The lower end of this was tacked down to the adjacent esophagus. The pack in the posterior mediastinum was left undisturbed. A rubber dam drain was inserted to the suture line of the esophagus. A few skin sutures were taken.

Postoperative course. The auricular fibrillation, which was more marked now, was controlled by the use of digitalone. Ten days after operation, the patient was taking fluids by mouth without regurgitation and was allowed a soft diet. About three weeks after admission, X-ray examination of the esophagus, with the aid of barium, failed to show any evidence of obstruction and no sacculation could be demonstrated in the upper dorsal or cervical region. Several days later, the gastrostomy tube was removed, at which time the neck wound was entirely healed. Before the patient

was discharged, larynx examination showed evidence of a left recurrent paralysis. His weight, which was 102 pounds on admission, reached 124½ pounds at the time of discharge.

On October 20, about five months after operation, the patient's weight was 175 pounds and the hoarseness which was present at the time of discharge from the hospital was entirely gone. Larynx examination on November 5 showed an entirely normal larynx. Reexamination of the esophagus with the use of barium showed the presence of a small residual diverticulum about two inches above the jugular notch. When the patient was last seen in the Follow-Up clinic on January 2, 1937, he had no symptoms referable to the esophagus. However, he did have manifestations of cardiac failure and was referred for therapy.

Pathological report described the surgical specimen as follows: The specimen consists of two portions of tissue which measure together 6 cm. in length and 3 cm. in width. The tissue is apparently a sac. It is lined on the inner layer by a flat two millimeter layer of pearly appearing epithelium. This is smooth throughout its entirety. It is surrounded by a layer of fibrous tissue and possibly a layer which is muscle tissue. Microscopically, tissue was composed of smooth muscle and connective tissue lined by squamous cells.

Case 2. History (Adm. 399463). The patient was a 54 year old tailor who was admitted to the hospital on October 8, 1936. His past history included bronchopneumonia in 1930, pleurisy in 1933, a right hernioplasty and three nasal operations twelve years ago. His chief complaint was post-prandial nausea of seven years' duration. This usually came on ten to fifteen minutes after a meal and was followed by regurgitation of food and occasionally by projectile vomiting of part of the recently ingested food. Five months before admission, he had some pulmonary symptoms, and a diagnosis of pleurisy was made. During this illness, an X-ray examination of the chest was taken and he was told that he had a "tumor" in the left anterior chest. Since that time, he had suffered from a variety of complaints, including precordial constriction, cough, expectoration of sputum, fever, peri-umbilical pain, and pain in the left anterior chest. These were all in addition to his chief complaint. He lost twenty pounds in weight since the onset of his illness, seven pounds of which were lost in the past five months. Although he never complained of anorexia, weakness and emaciation became progressively more marked.

Examination. The patient was an emaciated male with increased retro-manubrial dullness. The blood urea nitrogen was 15; the cholesterol, 335 mg. per cent; the sugar, 75 mg. per cent; the chlorides, 550 mg. per cent. X-ray examination of the esophagus showed the presence of a very large pulsion diverticulum which originated at the pharynx and esophagus. After six hour observation, most of the barium was still present in the sac.

Regurgitation of food continued during his stay in the hospital. Esophagoscopy was performed on October 15. A diverticulum about 4 cm. wide was entered, but the upper esophageal opening could not be found. The following day a Kader gastrostomy was performed. The patient was fed by gastrostomy and was instructed to irrigate his diverticulum, which he did by swallowing water and then regurgitating it spontaneously. One month after admission, diverticulectomy was performed.

Operation. Under avertin gas-oxygen ether anesthesia a liberal incision was made along the anterior border of the left sternomastoid with lateral

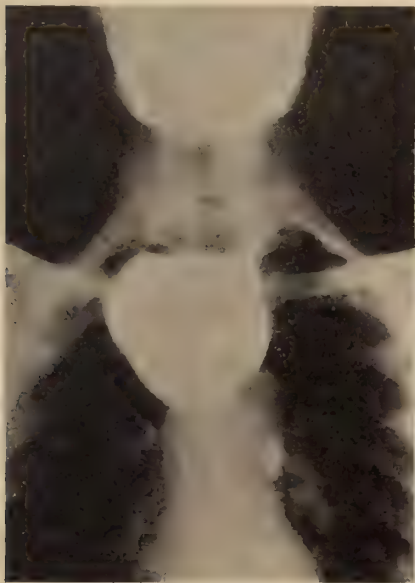


FIG. 3



FIG. 4

FIG. 3. (Case 2.) Preoperative film, showing the huge diverticulum almost completely filled with contrast medium. The esophagus below is not visualized.

FIG. 4. (Case 2.) Postoperative film with barium, showing a small residual pocket and the outline of the esophagus below.

retraction of the great vessels together with the muscle. The left lobe of the thyroid was isolated, drawn forward, and the middle thyroid vessels severed.

The diverticulum was then exposed by dissecting down to the esophagus. Its wall was recognized by its pallor. It was drawn up into the field with forceps and then progressively drawn up out of the wound, being freed by blunt and sharp dissection. The mediastinum was widely opened up as a result of its delivery from that space and a packing was placed into it.

When this large diverticulum had been, in part, delivered, the left recurrent nerve was seen to pass over it and in immediate proximity to it. In

order to avoid its severance, a retractor drew the nerve aside. The intimate relationship of recurrent nerve to the diverticulum was noteworthy.

The large flabby sac was now out of the wound and dissected down to a neck about one inch long on the lateral, or perhaps posterior, aspect of the esophagus directly behind the left thyroid lobe.

The esophagoscopist now passed an esophagoscope, but, despite many efforts together with the guidance of the end of the esophagoscope via the wound, he was unable to pass the instrument into the esophagus below the diverticulum. Accordingly, the instrument was kept in place and the diverticulum was ablated. The finger could now be introduced into the lower opening of the esophagus which lay eccentric, being anterior and lateral. The end of the esophagoscope could now be conducted into this orifice, but could not be pushed down any further. Obviously there was some narrowing of the esophagus below the lower orifice.

A three layer closure of the opening in the esophagus with chromic sutures was carried out, a small pouch being deliberately left in order to avoid too great a narrowing of the esophagus at this level. A pack, which was left in the mediastinum as soon as the latter had been opened up, was left undisturbed and an additional pack was placed into the dead space left by the removal of the diverticulum. The skin was closed about with drains.

Postoperative course. Soon after operation the patient could only speak in a whisper. Examination of the larynx showed the left vocal cord to be fixed and there was limitation of abduction in the right cord. Drainage from the tube in the neck was rather profuse postoperatively, and about ten days after operation it was found to be rather characteristic of chyle. The material contained 0.78 per cent lipoids, whereas chyle ordinarily contains 5 to 15 per cent. Examination of the neck after the introduction of radiopaque material showed this material to enter a cavity in the region of the diverticulum, and extending from this cavity, which showed a fluid level, was a thin trickle of radiopaque material which extended in irregular manner for a distance of about one inch to the left just above the clavicle. It was thought that this might very well be part of the thoracic duct. The discharge from the neck wound cleared up rapidly and the wound healed from below. An examination of the larynx while the patient was still in the hospital showed some motion of the left cord and a normal right cord. About three and a half weeks after operation, the gastrostomy tube was removed and at this time the patient was eating a soft diet without difficulty.

When seen in the Follow-Up Clinic on January 15, 1937, the patient had gained 20 pounds in weight and both the neck and abdominal wounds were healed. His only complaint at this time was a sense of tightness on swallowing.

The pathological report read as follows: the specimen consisted of a mass

received in fixative, measuring 5 by 4 cm. The external wall appeared smooth, shiny, and glistening. On opening the specimen, it consisted of a cystic structure, the wall of which measured 5 mm. in thickness. The inner lining was shiny in places and glistening; in other places the surface appeared to be roughened and somewhat irregular. Histological report: portion of the esophagus wall with chronic inflammation (diverticulum wall).

SUMMARY

The two cases herein described illustrate the rapidity with which extreme emaciation may develop as the result of a huge esophageal diverticulum. In these two instances, one-stage diverticulectomy brought about rapid improvement, followed by cure. The diverticulectomy was preceded by gastrostomy for feeding purposes; it was discontinued shortly after the diverticulectomy was performed. Careful preoperative treatment is stressed, especially lavage of the diverticulum. The operation itself is described in detail so as to bring out the meticulous care used in the prevention of a leak into the mediastinum, in the packing off of the mediastinum, and in the careful suturing of the esophageal wall with multiple layers of sutures. The esophagoscope was employed both as a guide in the dissection of the sac and the suturing of the esophagus after the diverticulectomy. The recurrent nerve was visualized and retracted. With these precautions a one-stage operation is quite safe. Moreover, the dissection of the sac is much cleaner in a one-stage procedure, since granulation tissue which forms between the two stages of the two-stage procedure is avoided.

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CONTUSION PNEUMONIA

SIDNEY BLUMENTHAL, M.D., AND BENJAMIN COPLEMAN, M.D.

[*From the Pediatric Service of Dr. Bela Schick and the Radiological Service of Dr. L. Jaches*]

Contusion pneumonia, i.e., pulmonary infiltration following trauma to the chest, has been described rarely in the English literature. Inasmuch as foreign observers have reported its occurrence in about 2 per cent of cases of children in whom there has been trauma to the chest, it is felt that the condition warrants emphasis.

History (Adm. 385133). A five and a half year old colored female, was admitted to the Pediatric Service on October 2, 1935. At about ten-thirty in the morning of the day of admission, while crossing the street, the child was struck by an automobile and apparently received an injury to the chest. She did not lose consciousness following the injury and there was no hemorrhage from the nose or ears. The child was brought to the hospital immediately. The mother stated that prior to the accident the child had been in good health. There had been no malaise or cough. The appetite had been good. She had been active and had shown no evidence of an impending illness.

On admission at eleven o'clock in the morning her temperature was normal. The patient complained of pain in the right chest. Physical examination was negative except that the child had many contusions and lacerations over both lower extremities as well as about the head, but none were noted about the chest. It was thought advisable to keep the child under observation, and in the succeeding hours it was noted that she became drowsy, but, when aroused, was markedly irritable. On any manipulation the child complained of very severe tenderness over the right chest. At four o'clock that afternoon her temperature rose to 101°F. and at five o'clock it was 101.4°. There was no cough.

At six o'clock the child appeared acutely ill. The respirations were rapid but there was no cyanosis. On percussion of the chest there was found definite impairment of resonance at the right base posteriorly with decreased breath sounds in this region and in the posterior axilla. No râles or friction rub were heard. The hemoglobin was 60 per cent; the red blood corpuscles, 3,800,000; and the white blood cells, 9,800, with 78 per cent polymorphonuclear leukocytes. An X-ray examination made eight hours after the injury showed no evidence of fractured ribs, effusion or pneumothorax, but it did show a shadow in the right lower lung field which was interpreted as pneumonia.

The next day the child still complained of considerable chest pain. There was marked limitation of motion of the right chest and tenderness over the right lower thorax. There was impaired resonance at the right base with many fine crackling râles anteriorly and in the right axilla. Late in the afternoon of the same day, the temperature dropped to normal and

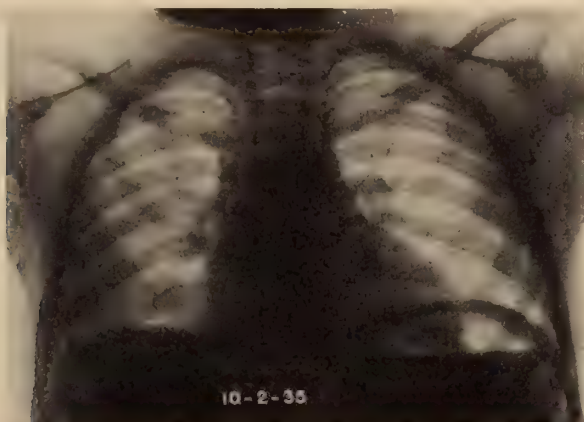


FIG. 1. Chest film taken eight hours after admission, showing lesion at right base

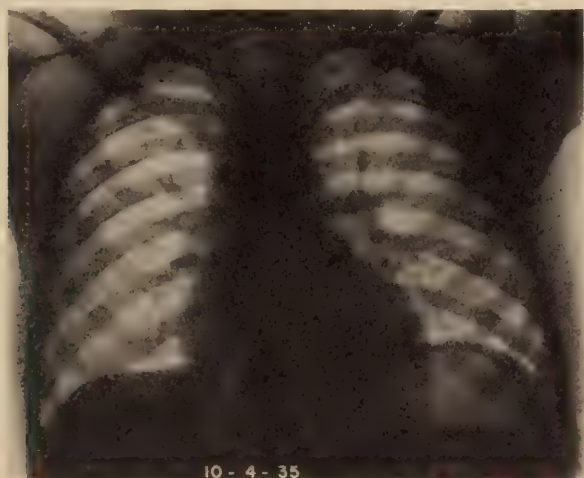


FIG. 2. Examination two days later; resolution following clinical improvement

during the remainder of the child's period of hospitalization she was afebrile. The white cell count was 10,200 with 75 per cent polymorphonuclear leukocytes. On October 4, the third day of illness, a striking change in the child's general condition was noted. The limitation of excursion of the chest and tenderness had disappeared. Impaired resonance, distant

breath sounds and many crackling râles were still present at the right base. A roentgenogram of the chest, taken that day, showed complete resolution of the process reported previously.

The child's convalescence was uneventful. The physical signs gradually cleared and she was discharged in good condition on October 11.

COMMENT

The diagnosis in this case was puzzling. The patient was admitted to the hospital immediately following injury to the chest. The history and physical findings at that time revealed nothing that could be interpreted as possible prodromata for the pulmonic lesion which followed. It is significant that the child's temperature remained within normal limits until five to six hours after the injury. The short course of the illness, together with the normal blood picture, suggest that the lesion was not one usually seen following an upper respiratory infection.

The occurrence of a pleural or subpleural hemorrhage, or pleural edema, was first considered, but the rapidity of the resolution was against this. It was felt that atelectasis could be ruled out by the absence of such criteria as mediastinal shift or elevation of the diaphragm. Since there was no edema of that portion of thorax, the possibility that the shadows seen were superimposed soft parts was dismissed.

Lauche considers that an interval of six to eight hours elapses between the time of trauma and the onset of clinically recognizable signs. Meltzer saw hepatization in a puppy four to five hours after experimental injury to the chest. The interval of six to eight hours is believed to be necessary for the development of the pathological process. The onset of signs and symptoms more than three or four days following the injury makes it unlikely that there is any direct pathological relationship between the two.

The nature of the lesion has been described as a fibrinous pneumonia. Experimentally, subpleural hemorrhages and even pulmonary tears have been demonstrated following trauma. The localization of the pneumonic process most often approximates the site of trauma, but it may occur anywhere in the chest irrespective of the locally traumatized site. Before the diagnosis of contusion pneumonia can be established, the presence of a respiratory infection antedating the trauma must be ruled out.

SUMMARY

Our patient had been well prior to the accident. When first seen, about one-half hour later, the outstanding feature noted was pain in the chest, suggesting a fractured rib. The pulmonic lesion developed at the site of the pain, in the lower right chest. In addition to these facts, the normal temperature for five or six hours and the short course of the illness lead us to believe that this is a typical example of contusion pneumonia.

Note. Since the above case was submitted for publication another somewhat similar case has been observed.

A colored male (Adm. 419642), aged 11, was struck on the lower left chest with a stick, four days prior to admission on January 31, 1938. He complained of pain on respiration, slight cough, and marked tenderness over the left lower ribs anteriorly.

His temperature was normal, and no signs of pulmonary changes could be elicited on physical examination.

X-ray examination failed to show any evidence of fracture of the ribs, but a faint shadow was noted at the lower portion of the left lung. A Roentgen differentiation between a pleural exudate and an intrapulmonary lesion could not be made.

He was discharged from the accident ward on the same day.

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CLINICAL PATHOLOGICAL CONFERENCES

GEORGE BAEHR, M.D., AND PAUL KLEMPERER, M.D., *presiding*

Wednesday, October 13, 1937

Case 1. Pulmonary Thrombophlebitis Secondary to Chronic Lung Abscess

(From the Medical Service of Dr. George Baehr)

History (Adm. 412923). A white male, aged 37 years, entered the hospital with a history of having had an upper respiratory infection at the age of 30, characterized by a frequent cough, productive of small amounts of mucoid sputum. The cough gradually increased in frequency and severity, and became more productive. The daily expectoration finally averaged two ounces of grayish foul sputum.

In December 1930 he entered another hospital where the diagnosis of bronchiectasis was made. As his symptoms continued, he was readmitted to the same hospital in February 1931. At this time a diagnosis of "abscess of the right lower lobe" was made. He left the hospital, although his symptoms were still present and his expectoration was profuse. Three weeks later he entered a second hospital where a diagnosis of "calcified lung abscess" was made. In September 1931 he entered a third hospital where he was bronchoscoped. His sputum continued to be foul and increased in quantity to fifteen cupfuls daily. A thoracotomy of the right posterior chest was then performed with the removal of some "lung tissue". Subsequent to this operation, he became afebrile and his cough and sputum diminished. Six months later (March 1932), he reentered that same hospital because of recurrence of his cough and sputum. A second thoracotomy was performed; the lung was repeatedly aspirated, but no pus was obtained.

On recovering from the second operation the patient returned to work, but continued to raise one to one and a half cupfuls of foul sputum daily, mainly after an early morning coughing paroxysm. He had been afebrile except for a short period six months before admission to The Mount Sinai Hospital, but during the three months preceding his entrance to the hospital his cough and the quantity of sputum had increased. For the last four weeks there had been increasing exertional dyspnea. Five days before admission he was seized with a chill which lasted about ten minutes, and which was associated with high fever and hoarseness. This episode was followed by an even more marked increase in cough and sputum. The fever persisted with daily fluctuations from 100° to 106°F. and was accompanied by chills. During the preceding three days his sputum had been blood-streaked and there was moderate dyspnea and orthopnea.

Examination. The patient appeared to be chronically ill. There was a foul odor to his breath. The tonsils were buried and contained a caseous exudate. There was a well healed lower thoracotomy scar below the angle of the scapula. Above and below the thoracotomy scar the breath sounds were diminished and the voice sounds increased. Subcrepitant râles were audible throughout the right lung, especially in the region of the thoracotomy. The temperature was 101°F.

The blood pressure was 120 systolic and 64 diastolic. The respiratory rate was 22 per minute. The fingers were moderately clubbed.

Laboratory Data. The hemoglobin was 78 per cent; the white blood cells, 17,200 per cu. mm., with 87 per cent polymorphonuclear leucocytes and 7 per cent lymphocytes. The blood Wassermann test was negative. The erythrocyte sedimentation rate was 27 minutes. Blood urea nitrogen was 27 mg. and blood sugar, 125 mg. per 100 c.c. Urine analysis revealed a faint trace of albumin and an occasional granular cast. A roentgenogram of the chest showed a diffuse pneumonic process in the right lower and middle lobes with evidence of cavitation at the apex of the right lung and in the right lower lobe. In the anterolateral portion of the right chest was a shadow which suggested the presence of a pyopneumothorax.

Course. A chest aspiration failed to reveal the site of the abscess and operation was therefore deferred. On the day following admission, the patient became intensely dyspneic, cyanotic and coughed up large quantities of very foul sputum. His temperature, which had been normal, became spiking in character and rose to 105.6°F. At the same time embolic phenomena became manifest in the fingers and toes, which became discolored and cold. His condition from this time on declined progressively, with death occurring on the sixth day in the hospital.

Necropsy Findings. There was an elliptical elevated bluish area on the medial aspect of the right fifth toe and a similar area involving the distal half of the terminal phalanges of the left index finger. The pleura of the right lung was thickened. There was a hard calcific subpleural nodular mass (3 cm. in diameter) located near the hilum of the right lower lobe. The bronchi of the right upper and right lower lobes showed a marked cylindrical dilatation. There was a spherical cavity 6 cm. in diameter in the central portion of the right lower lobe lateral to the calcified mass described above. The cavity had a thin fibrous capsule and was filled with a dark green, semi-fluid, foul smelling material. The walls of the cavity were smooth and lined by necrotic material. A gray, adherent thrombus was found in a branch of the pulmonary vein lying on the posterior surface of the large cavity described above. There was also a number of small cavities filled with a thick, creamy, purulent material in the peripheral portion of the paravertebral segment of the right lower lobe. The right lower lobe showed extensive fibrosis. In addition, there was a small 0.5 cm. cavity in the middle of the right upper lobe which opened directly into a bronchus and patchy bronchopneumonia of the right lower lobe.

The heart, liver and kidneys contained numerous small metastatic abscesses. Smears of pus from the abscesses showed gram-positive cocci which did not grow and could not, therefore, be further identified.

Comment. Dr. Baehr called attention to the fact that the patient had a lung abscess seven years before admission, which had been inadequately treated at that time. He stressed the important point that operation for an anaerobic lung abscess should include the formation of a bronchial fistula for adequate aeration of the abscess cavity and that the fistula should be allowed to remain open until infection has been controlled. In the opinion of Dr. Baehr, the recurrence of symptoms three months before death was coincident with an extension of the process from an undrained focus. On admission the patient was considered to have had a diffuse gangrenous bronchopneumonia spreading throughout the right lung. A chest aspiration was done to rule out intrapleural suppuration because of the roent-

genographic suggestion of an encapsulated pyopneumothorax. In view of the negative tap, it was concluded that the shadow represented a thickened pleura. Terminally the clinical picture of chills and fever associated with embolic phenomena in the extremities suggested a thrombophlebitis of the pulmonary veins.

Dr. Klemperer pointed to the unusual feature in this case, which was the finding of a thrombophlebitis of the pulmonary vein. This not infrequently is seen in cases of acute lung abscess but is an uncommon finding in cases of chronic lung abscess. He recalled two cases in which multiple liver abscesses were associated with a chronic lung abscess. The bacteria were found in the heart, liver and kidneys. There were no lesions of the heart valves. Dr. Klemperer explained the early X-ray report of a "calcified lung abscess" by the presence of a large primary calcified tuberculous infect near the abscess, and said that lung abscesses are rarely calcified.

Case 2. Coronary Artery Thrombosis with Myocardial Infarction. Hemopericardium due to Rupture of the Heart

History (Adm. 406447). The patient, a 69 year old white male, entered the hospital with the history of an attack of upper abdominal pain four years previously, which lasted one-half hour and radiated to the precordium. Sharp, transitory chest pain had recurred for several years and he had had intermittent claudication for the past two to three years. There was no history of venereal disease. Two years before admission he developed pollakiuria, urgency, nocturia, difficulty in starting the stream, and pain just before the onset of micturition. All these symptoms increased progressively during the six months prior to his admission.

Examination. The patient was a fairly well developed, chronically ill, white male. The chest was barrel shaped; the lungs, hyperresonant. The left border of the heart was percussed at the mid-clavicular line. There was a harsh apical systolic murmur transmitted to the axilla, which partially replaced the first sound. A short systolic murmur, transmitted upward, was heard over the aortic area. The second aortic sound was louder than the second pulmonic. The heart rhythm was regular, with frequent premature ventricular contractions. The pulse rate was 84 per minute. The blood pressure was 192 systolic and 102 diastolic. The prostate was enlarged to one and one-half times the normal size; the right lobe was irregularly nodular and quite firm.

Laboratory Data. The blood hemoglobin was 74 per cent; the white blood cells, 9,700 per cu. mm., with 72 per cent polymorphonuclear leucocytes. The blood Wassermann reaction was negative. The blood urea nitrogen was 17 mg. and the blood sugar, 85 mg. per 100 c.c. The electrocardiogram showed changes which were interpreted as indicating a previous, possibly a recent, coronary occlusion.

Course. The patient was afebrile. A cystoscopy was performed soon after admission and three ounces of residual urine were obtained. The bladder mucosa showed a low grade cystitis with moderate trabeculation and intravesical intrusion of the middle and lateral lobes. The prostate was irregularly enlarged and firm.

A bilateral vas ligation was done four days after admission. Three days after this procedure an electrocardiogram showed progressive changes. The patient, however, had no cardiac symptoms, except for a fall in blood pressure, now recorded as 155 systolic and 70 diastolic. He was, however, weak and apathetic. In view of these developments, further surgery was no longer considered and an indwelling catheter was therefore inserted.

Seventeen days following admission the patient developed edema and pain in both testicles. Twenty-nine days after admission, while voiding, he was seized with a severe constant constricting pain at the lower border of the sternum, which was associated with profuse perspiration. The blood pressure at this time was 180 systolic and 90 diastolic. The white blood cells numbered 9,400, with 89 per cent polymorphonuclear leucocytes. During the next five days he had repeated attacks of precordial pain, pallor, and cold sweats. At no time was a friction rub heard. Death occurred suddenly while the patient was asleep, six weeks after the onset of precordial pain.

Necropsy Findings. The pericardial sac contained 400 c.c. of partially clotted blood. The heart was moderately enlarged and weighed 430 grams. A subepicardial collection of blood, measuring 4 by 1 by 0.5 cm. was found beneath the left auricular appendage at the auricular ventricular junction in the coronary sulcus on the anterior aspect of the heart. This hematoma separated the layers of fat and dissected partially around the coronary sinus along the ramus anterior sinistri ventriculi of the left circumflex coronary artery, passing deeply as a tract between the myocardium and epicardium on the anterior longitudinal sulcus of the left ventricle, two-thirds of its distance to the apex.

The septal wall was found to be thin and gray on cut section and consisted, in the main, of dense fibrous connective tissue. The ventricular wall forming the apex also showed a diffuse fibrosis. The left ventricle was markedly dilated. The ventricular muscle of the anterior wall, just beneath the subepicardial collection of blood, was flabby and, on cut section, appeared a dull, yellowish gray, with a few small linear red areas. These areas of softening between the columnae carneae contained a very narrow zone of rupture which extended through two-thirds of the thickness of the wall and measured about one millimeter. The coronary vessels were markedly sclerotic and narrowed by intimal plaques. This reaction was especially pronounced in the anterior descending branch of the left coronary artery, one inch from its origin, where its lumen was pin-point. The left circumflex artery was completely occluded by a fresh thrombus superimposed on an arteriosclerotic plaque.

The *aorta* showed marked atherosclerotic changes with ulceration. The aorta was markedly dilated below the origin of the renal vessels. At that point it widened to 5 cm. in diameter for a distance of 18 cm. A thick red shaggy thrombus was adherent to the wall over a markedly thinned and irregularly ulcerated surface. The kidney capsules stripped with some difficulty revealing a moderately granular red and speckled yellow surface with occasional cortical cysts. The cortex was thin and poorly demarcated from the medulla. There were no other significant findings.

Comment. Dr. Klemperer stated that the fibrosis of the left ventricle was due to severe obliteration of the anterior descending branch of the left coronary artery. It was clear that the source of epicardial hemorrhage was from the wall of the left ventricle near the ramus margo obtusus, the result of a recent thrombosis of the main left coronary artery.

Dr. Baehr referred to the significant observation that, on admission, there was neither angina pectoris, heart failure, nor any clinical evidence of coronary occlusion. Repeated electrocardiograms after operation revealed progressively increasing changes which indicated that a recent thrombotic occlusion had occurred, probably at the time of the operation or shortly thereafter. This is a not uncommon

mon occurrence during or after operations upon elderly persons. Twenty-five days later, a second coronary thrombosis or extension of the thrombosis occurred. The patient died suddenly six days later, due to rupture of the heart. By the sixth and seventh days after a coronary occlusion, myomalacia is well advanced and this is the time when rupture of the heart is apt to occur.

Case 3. Carcinoma of the Stomach

(From the Surgical Service of Dr. Ralph Colp)

History (Adm. 411387). The patient was a 32 year old white male who was well up to two weeks before his first admission to the hospital. At that time he experienced a sudden sticking post-prandial epigastric pain. This sensation persisted for a week, when he suddenly became nauseated and vomited some dark brown material. Shortly thereafter he became dizzy and vomited large amounts of frank blood. He became very weak and pallid. The next day his stools were tarry. He returned to work for four days, but on the thirteenth day after onset of his illness vertigo, weakness and nausea reappeared.

Examination. The patient was a well developed and well nourished, pale white male. His temperature was 100.4°F.; his pulse rate, 104 per minute. The lungs were clear and the heart was negative. The blood pressure was 130 systolic and 80 diastolic. There were no abdominal tenderness or masses. Rectal examination revealed the presence of a tarry stool.

Laboratory Data. The blood hemoglobin was 50 per cent; the red blood cells, 3,190,000; the white blood cells, 5,000 per cu. mm., with 67 per cent polymorphonuclear neutrophils, 30 per cent lymphocytes and 3 per cent monocytes. The blood Wassermann reaction was negative. The guaiac test for blood in the stool was 4 plus. The urine was negative, except for the presence of urobilin in a dilution of 1 to 80.

Course. The patient was placed on a Meulengracht diet and given iron ammonium citrate. The stools became guaiac negative after twenty days. A gastro-intestinal series showed a slight deformity of the duodenal bulb. This alone was not considered sufficient for an X-ray diagnosis of ulcer. The blood hemoglobin rose steadily to 76 per cent and the patient was discharged after twenty-five days in the hospital.

Interval History. In spite of continued strict adherence to the Sippy regime he began to experience a constant dull aching epigastric pain which radiated through to the back. This was associated with nausea unrelated to food and not relieved by alkalies. He lost twenty-five pounds in weight during this period. There had been neither nausea nor hematemesis. The patient was readmitted two months after discharge because of severe epigastric distress.

Second Admission. The patient was a well developed, well nourished, white male. The temperature was 100.4°F. The only positive physical finding was slight epigastric tenderness. The blood pressure was 125 systolic and 80 diastolic.

Laboratory Data. The blood hemoglobin was 87 per cent; the white blood cells, 15,950 per cu. mm., with 88 per cent polymorphonuclear leucocytes, 8 per cent lymphocytes and 12 per cent monocytes. Urine analysis was negative. The stools showed a 3 plus guaiac reaction. Free hydrochloric acid could not be demonstrated in two gastric aspirations. Another gastro-intestinal series revealed a small per-

sistent oval patch of barium, which was present in the cardiac end of the stomach on the posterior wall, the appearance of which resembled that of a small penetrating ulcer.

Course. In view of the lack of response to medical management and the presence of increasing abdominal pain, fever, leucocytosis and persistent guaiac positive stools, operation was agreed upon. Two weeks after admission he suddenly vomited about two ounces of bright red blood. His blood hemoglobin dropped from 75 per cent to 50 per cent. His temperature rose to 103.4°F. and his stools again became tarry. Five days after this episode he was given a blood transfusion and operated upon.

At the operation, a hard nodular mass was found to occupy the lesser curvature of the stomach near the cardia, and to extend up toward the esophagus. It appeared to be extrinsic and occupied only a small part of the stomach. In view of the gastric anacidity, a posterior gastro-enterostomy was done. The exact nature of the lesion could not be ascertained at operation.

The patient's postoperative course was febrile and marked by frequent massive, almost exsanguinating, gastric hemorrhages. Despite eleven transfusions and shock treatment, he died sixteen days postoperatively, almost four months after the onset of his symptoms.

Necropsy Findings. The stomach was filled with 1,250 c.c. of fluid and clotted blood. At the terminal portion of the esophagus, a small grayish black, succulent, sessile mass was found situated along the edge of a large ulcerated carcinoma 15 cm. in diameter. The base of the tumor was formed by the inferior aspect of the liver and the anterior aspect of the pancreas. A few enlarged lymph nodes were found along the lesser curvature of the stomach. On section, these revealed a diffusely gray background with scattered yellow granules. The gastro-enterostomy was patent and well healed. The peri-esophageal and periaortic lymph nodes also showed carcinomatous deposits. The lungs showed two small metastatic carcinomatous foci. The liver showed no evidence of metastases.

Comment. Dr. Baehr recalled that the X-ray examinations showed a suspicious lesion of the cardia and that, clinically, there was no response to medical ulcer therapy. In addition, no free hydrochloric acid could be demonstrated in repeated gastric analysis. In retrospect, it seems that the diagnosis of carcinoma should have been made before operation. Peptic ulcer of the duodenum is almost never observed in patients with achylia gastrica, and gastric ulcer rarely. The finding of an achylia gastrica should therefore have provided adequate grounds for predi-
cating the existence of a malignant ulceration as the cause of the hematemesis.

Reported by B. GITLITZ, M.D.

Wednesday, October 20, 1937

Case 4. Multiple Carcinomas of the Colon

(From the Surgical Service of Dr. Ralph Colp)

History (Adm. 408130). The patient, a 67 year old white female, entered the hospital because of post-prandial pains, anorexia, nausea, vomiting and a weight loss of thirty-five pounds—all of four and a half weeks' duration. Three weeks

prior to hospitalization she had become markedly constipated for several days and, following this, suffered from severe watery diarrhea.

Examination. The patient was flushed and lethargic. There were numerous coarse crackling râles at the left base. The heart revealed no abnormalities. The blood pressure was 116 systolic and 70 diastolic. The abdomen was moderately distended and doughy. In the right lower quadrant there was a freely movable, poorly defined mass. It was non-tender and the size of a grapefruit. A similar mass, orange-sized, was felt in the umbilical region.

Laboratory Data. The hemoglobin was 70 per cent; the white cells, 13,400 per cu. mm., with 88 per cent polymorphonuclear neutrophils. The stool gave a one plus guaiac reaction. The urine was negative. A barium enema showed a stenosing lesion at the splenic flexure.

Course. Although bowel movements continued, the abdomen became tremendously distended, so that a cecostomy was performed. The drainage from this opening was profuse and the patient began to improve. However, the blood urea nitrogen mounted to 118 mg. per 100 c.c. With forced fluids and a transfusion, the urea nitrogen dropped within four days to 67 mg. On the fifth day after operation, generalized abdominal tenderness and signs of left lower lobe bronchopneumonia appeared. The patient declined rapidly, and died on the sixth postoperative day.

Necropsy Findings. There were stout intercolonic adhesions. Three small yellow submucous nodules were found in the ascending colon. The transverse colon, about 8 cm. distal to the hepatic flexure, was constricted by a tumor which formed an annular thickening in the wall of the colon. The mucosa over the tumor was ulcerated and discolored. Within the thickened transverse mesocolon several lymph nodes were found. In the descending colon, just distal to the splenic flexure, another mass was discovered. This was flat, infiltrating and had a nodular, dirty red, granular surface. In the mucosa of the proximal end of the sigmoid, there was a third mass, also flattened, fungating and penetrating the muscularis. In addition, two small pedunculated polyps were found between the last two tumors. Metastatic carcinoma was found in the omentum, mesenteric and peripancreatic lymph nodes. There was also a fibrinopurulent peritonitis.

Comment. Dr. Klemperer pointed out that two types of carcinoma of the colon were present in this case. One type (adenocarcinoma) had produced no metastases, while the other (scirrhous) had spread to other organs. In discussing the relation of polypoid adenomata to carcinoma, he said that there is hardly any doubt that polyps of the colon may become carcinomatous. The question is:—How often does this occur? In one thousand cases of colons removed for carcinoma at The Mount Sinai Hospital, the incidence of polyps was 6.2 per cent. However, in one thousand routine autopsies it was 6.6 per cent, with the greatest frequency up to 16.4 per cent in the older age groups. These figures do not warrant the conclusion that polyps are likely to become frequently malignant. It should be remembered, however, that in the surgical material only a small part of the colon was available for study. Dr. Baehr felt that there was something wrong about these statistics, for clinical experience indicates that carcinoma is very apt to develop in adenomatous polyps of the stomach and the colon. In fact, carcinomatous transformation is found not infrequently in several polyps in the same stomach or colon.

Case 5. Rheumatic Myocarditis with an Unusual Course and Without Clinical Manifestations of Valvular Disease

(From the Medical Service of Dr. George Baehr)

History (Adm. 409008). The patient, a 37 year old white male, who was athletic and enjoyed good health, entered the hospital for the first time in 1935 complaining of dyspnea, continual cough and frequent expectoration of blood-tinged sputum of approximately one year's duration. In November 1934, he suddenly developed high temperature, general prostration and a non-productive cough. It was diagnosed as influenza. Following this he continued to suffer from fever, night sweats, orthopnea, dyspnea and hemoptysis until he entered the hospital.

Examination. The patient was well developed, ruddy, markedly dyspneic and cyanotic. The anteroposterior diameter of the chest was increased. The lungs showed slight dullness, diminished breath and voice sounds, and crackling râles over both bases. No cardiac murmurs were heard, nor was the heart enlarged. The sounds were of good quality with accentuation of A2. The blood pressure was 130 systolic and 80 diastolic. No ascites was present.

Laboratory Data. The hemoglobin was 72 per cent; the red blood cells, 5,900,-000; white cells, 10,000 per cu. mm., with 62 per cent polymorphonuclear neutrophils. The urine and Wassermann tests were negative. Circulation studies revealed a venous pressure of 15.5 cm. per cu. mm., a saccharine circulation time of 27 seconds and vital capacity of 2,700 c.c. The electrocardiogram showed regular sinus rhythm, left ventricular preponderance, P waves wide and notched, QRS of high voltage and slurred, T1 inverted and T2 low. Chest X-ray examination disclosed a generally enlarged heart with flattened contour as in myocardial disease. The roentgenograms of the lung showed evidence of marked congestion. Bronchocopy was negative.

Course. After the patient had been in bed several hours, a gallop rhythm became audible. With restriction of fluids and the use of mercurial diuretics, the patient lost fifteen pounds in two weeks and his cough, dyspnea and hemoptysis all subsided. Dr. Rabin pointed out that the small pellets of rather pale, bloody sputum, often rusty colored, suggested an origin within the lung rather than in the bronchial tree. He further stated that such bleeding is seen in severe chronic myocardial disease. The etiology of the patient's cardiac disease remained obscure. He was thought to have some unusual form of myocardial infection. The exact nature of the febrile episode occurring a year before admission could not be determined. The patient left the hospital against advice before a definite diagnosis could be made. He returned to work but again developed congestive failure and reentered the hospital.

Second Admission (December 2 to 25, 1935). During this admission a systolic murmur was heard for the first time to the left of the sternum, in addition to a persistent gallop rhythm. The patient lost twenty pounds under diuretics and dietary restriction, but again left against advice after three weeks. At this time he was considered to have rheumatic myocarditis, although definite evidence of mitral stenosis was not present.

Third and Fourth Admissions (January 6 to 10 and November 25 to December 13, 1936). In the eleven months following the third admission the patient was bedridden with severe dyspnea most of the time and was readmitted twice in con-

gestive failure. During the fourth admission various etiologies for the myocardial disease were suggested, including interstitial myocarditis (Fiedler's myocarditis), adherent pericardium, rheumatic carditis, coronary artery disease, Von Gierke's disease and beri-beri heart. The majority opinion, however, was in favor of the first diagnosis, that is, interstitial myocarditis (of Fiedler).

Fifth Admission (May 23, 1937). Following his discharge eight months previously, the patient was observed in the Presbyterian Hospital for two months where he displayed edema extending as high as the sacrum. This diminished with bed rest. He was told that he had auricular fibrillation. After two months in the hospital he was allowed to return home and to work. Six weeks before his readmission to The Mount Sinai Hospital he was forced to stop work because of recurrence of his symptoms (dyspnea, orthopnea, slight cough and occasional hemoptysis). In addition, he had begun to have severe "lightning" pains, beginning in the thigh and radiating down both legs.

Examination. He was acutely ill, dyspneic, orthopneic and cyanotic. The neck veins were full. The breath sounds were diminished at both lung bases posteriorly with râles at the left base. The heart was markedly enlarged to the left, and the right percussion border was one inch to the right of the sternum. Sounds were of good quality, with P₂ greater than A₂ and accentuated. No murmurs could be heard. The rhythm was irregular. The abdomen was extremely tender but contained no clinically detectable fluid. The liver edge was felt six finger-breadths below the costal edge. There was markedly diminished vibration, position, pain and temperature sense in the feet. Myocarditis of unknown etiology, with auricular fibrillation, congestive heart failure and peripheral neuritis on the basis of dietary deficiency, was the best possible diagnosis.

Laboratory Data. The hemoglobin was 68 per cent; the red blood cells, 4,000,000; the white blood cells, 8,900 per cu. mm. Sedimentation time was one hour and forty minutes. The venous pressure was 11, rising to 17 on right upper quadrant pressure. Saccharine time was 32 seconds. Electrocardiographic studies revealed no change from the previous readings except for fibrillation.

Course. During the final stay in the hospital his temperature varied between 99° and 100°F. He was given large doses of Vitamin B, in the hope that the "lightning" pains, which were attributed to his low caloric, low vitamin diet, would be relieved. There was no clinical response to this therapy, however. Digitalis, mercurial diuretics and heavy sedation failed to help him. His dyspnea increased, the liver became enlarged, and he died in pulmonary edema. At the time of death, a diagnosis had not been definitely reached and he was considered to have an idiopathic myocarditis.

Necropsy Findings. The heart was greatly enlarged, particularly the left side, with hypertrophy and dilatation of all chambers. It weighed 640 grams. There was slight thickening of the endocardium of the right side of the heart. The tricuspid valve was clear, except for a few isolated areas of thickening along the free margin. The endocardium of the left atrium showed definite areas of roughening on the posterolateral aspect. The anterior leaflet of the mitral valve presented many well defined, gray-yellow, thickened, opaque areas two to three millimeters in diameter. The valve cusps were vascularized and showed slight thickening in isolated areas along the free margins. The chordae were grossly normal. The aortic valves showed conspicuous changes. The leaflets were thickened and the

left posterior commissure was partially absorbed, producing a bicuspid valve. The right leaflet did not terminate sharply at its left margin, but instead it formed an annulus several millimeters wide which extended around the coronary ostium and became lost in the aorta. The valvular lesion caused stenosis and insufficiency. The ventricular endocardium was thickened. The myocardium was pale brown with many small, white and yellow patches just beneath the endocardium. The coronary vessels showed many intimal atheromatous plaques which, however, did not compromise the lumina. Microscopic examination revealed evidences of an acute, as well as an old, rheumatic process in the myocardium. There was an organized pericarditis over the right auricular appendage. The lungs showed congestion and edema and, in the right lower lobe, bronchopneumonia.

Comment. Dr. Klemperer summarized the case as one of rheumatic carditis with an unusually extensive myocardial involvement and slight, but definite, valvular lesions, both chronic and acute. Dr. Baehr pointed out that the patient had not presented the circulatory dynamics of aortic stenosis and offered the opinion, therefore, that the chronic heart failure could be ascribed to recurrent rheumatic myocarditis. He said, however, that diffuse interstitial myocarditis, though a rare disease and therefore difficult to diagnose, may result in a colossal hypertrophy of the heart. In this instance the myocarditis was unquestionably of rheumatic origin. Because of the absence of murmurs and of the characteristic disturbances in circulatory dynamics, the associated valvular lesion was not recognized clinically and the rheumatic etiology was only proved at autopsy.

Dr. Oppenheimer, on the other hand, felt that aortic stenosis might have contributed to the fatal outcome and alluded to the fact that stenosis is frequently silent for long periods.

Dr. Master was also of the opinion that the aortic lesion played a rôle, because of the left ventricular preponderance.

*Case 6. Double Carcinoma of the Colon in a Case of Chronic Ulcerative Colitis.
Subacute Combined Sclerosis*

(From the Medical Service of Dr. George Baehr)

History (Adm. 408377). The patient, a 42 year old Hungarian housewife, fifteen years before admission to the hospital, developed bloody diarrhea and fever. This persisted for eight years and thereafter was followed by frequent attacks of diarrhea without apparent bleeding, which recurred until she entered the hospital.

First Admission. The patient was first seen at this hospital in 1925. She was then told that she had "dysentery and colitis".

Second Admission. Two months prior to her recent admission she developed progressive weakness, pallor and loss of weight. This was followed by the development of post-prandial epigastric pain which was associated with vomiting, and was relieved by sodium bicarbonate. Her abdomen was noted growing progressively larger.

Examination. The patient was a thin, pallid, sub-icteric, chronically ill-appearing woman. There were bilateral lenticular opacities. The tongue appeared moderately smooth. Small, hard, discrete, movable nodes were palpable in both supra-clavicular fossae. Moderately dilated veins were present over the lower thorax and abdomen. There were dulness and diminished breath sounds at both bases.

Heart sounds were of poor quality. The blood pressure was 75 systolic and 50 diastolic. The abdomen was slightly distended with a pouting umbilicus and there was a fluid wave and shifting dullness. A firm liver edge was felt three finger-breadths below the right costal margin. The edge of the spleen was palpable four finger-breadths below the left costal margin. Rectal examination could not be made because of pain. There was moderate pretibial and sacral edema. The deep reflexes were active and there was a right Babinski sign. Position sense in the feet was reduced. At that time the patient was considered to have abdominal carcinosis secondary either to gastric neoplasm or to carcinoma developing in a polyp of the colon. The neurological signs suggested a subacute combined sclerosis.

Laboratory Data. The blood count was: hemoglobin 42 per cent; red blood cells, 3,740,000; white blood cells, 23,200 per cu. mm., with 86 per cent polymorphonuclear neutrophils; reticulocytes, 2.2 per cent; platelets, 160,000 per cu. mm. The urine showed a trace of albumin, a few white cells and a trace of bile and urobilin. The blood urea nitrogen was 56 mg.; the cholesterol, 205 mg.; the cholesterol ester, 20 mg. per 100 c.c.; the icteric index, 21; bilirubin, 1.6 mg. per 100 c.c.; Van den Bergh delayed positive; the total protein, 5.6 per cent (albumin 2.6, globulin 3.0).

A barium enema revealed the presence of marked ulcerative colitis involving the entire large bowel with areas of narrowing in the descending, distal transverse and ascending portions. There was no evidence of active ulceration. A chest X-ray examination was negative.

Abdominal tap several days after admission yielded clear yellow fluid in which no tumor cells could be demonstrated.

Course. The patient ran an afebrile course. The abdominal veins became increasingly more prominent, and portal thrombosis was thought to be responsible for the ascites and the collateral circulation. She became steadily weaker and more apathetic. Five days after admission the abdomen suddenly became more enlarged, anasarca increased and icterus deepened. With this, she became more emaciated; blood urea nitrogen rose to 65 mg. per 100 c.c. Death occurred on the fifteenth hospital day.

During her stay in the hospital there had been considerable speculation over the possible relationship between the chronic ulcerative colitis and carcinoma of the colon. Several other instances of colonic carcinoma associated with inflammatory polyposis had been observed in this hospital. The possibility of a relationship between her long standing chronic ulcerative colitis, smooth tongue and posterolateral column sclerosis was also entertained. These phenomena were ascribed to a food deficiency.

Necropsy Findings. The middle third of the ileum showed several shallow ulcerations covered with a red necrotic membrane. The mucosa of the large intestine was, for the most part, flat, atrophic and gray to reddish brown in color. The wall was distinctly thickened throughout. In the ascending colon, just proximal to the hepatic flexure, was a flat, sessile, firm, gray tumor three centimeters in diameter. Several red flat mucosal polyps two to six millimeters in length were seen just beyond the hepatic flexure. In the central portion of the transverse colon was an ulcerated, irregularly oval tumor measuring four by five centimeters. The descending colon contained an area of ulceration two to three centimeters in extent. Within this there were portions of non-ulcerated mucosa. The lungs showed

numerous areas of bronchopneumonia. The liver parenchyma was extensively replaced by metastatic tumor nodules. A group of enlarged matted lymph nodes surrounded the choledochus at the head of the pancreas, but the duct was patent throughout.

Comment. Dr. Klemperer felt that the carcinoma had developed from atypical regeneration of the intestinal epithelium following its destruction by ulcerative colitis. Microscopic sections were shown demonstrating areas of normal mucosa, mucosa with atypical and with frankly carcinomatous glands. He further stated that this was the first case of ulcerative colitis which he had seen give rise to carcinoma. He warned against accepting statistical evidence on the relation between carcinoma of the colon and any other disease, since this condition is found with such frequency in routine autopsy material (4 per cent in this hospital).

Dr. Baehr said that the polyps which give rise to carcinoma are usually of the adenomatous, rather than the inflammatory, type. In this case, the carcinoma had developed in a person who had clinically recovered from a prolonged chronic colitis.

Dr. Crohn pointed out that, if more cases of ulcerative colitis were cured, more would probably live long enough to become victims of carcinoma.

In answer to a question on the cause of jaundice in this case, Dr. Klemperer stated that it was the result of the very extensive liver metastases, in combination with compression of the bile duct by enlarged hilus lymph nodes.

Dr. Baehr reemphasized the observation illustrated by this case, that prolonged chronic colitis may be responsible for the occurrence of deficiency phenomena. The deficiency in diet and in assimilation were probably responsible for the tongue phenomenon and for the subacute combined sclerosis of the cord.

Reported by ARTHUR W. SELIGMANN, JR., M.D.

CLINICAL NEUROPATHOLOGICAL CONFERENCE*

JOSEPH H. GLOBUS, M.D., *presiding*

Monday, February 14, 1938

Case 1. Spongioblastoma of the Left Cerebral Hemisphere. Dr. Mark Kanzer

History (Adm. 388478). The patient, a man aged 57 years, entered the hospital on January 4, 1936. Apart from frontal headaches at long intervals of time, he was fairly well until three months prior to his admission to the hospital, when his headaches became more frequent and more severe and had localized to the region above the left eye. The pain was described as "hammering"; it was constant and did not radiate. The patient became emotionally unstable, being alternately irritable and apathetic. Five weeks later an intermittent stabbing pain developed in the left occipital region. At this time, pyorrhea was noted and many teeth were removed. Almost immediately the pain in the occiput disappeared and that over the left eye diminished. Soon after, however, the patient became troubled by the occurrence of nausea and vomiting when suddenly assuming the upright position. More recently, he had begun to display mental disturbances. In the course of his illness, which was marked by increasing weakness, he lost about fifteen pounds in weight.

Examination. The patient was poorly nourished and appeared to be chronically ill. He was dull and apathetic. He was aware of mental difficulties and of impairment of memory for recent events. There was generalized percussion tenderness of the skull. There was a questionable left hyposmia. The right palpebral fissure was wider than the left. The right pupil was slightly larger than the left. Both pupils were irregular, but reacted well to light and in accommodation. There was bilateral limitation of lateral gaze. Vision was slightly reduced in both eyes. There was bilateral papilledema with retinal hemorrhages, both conditions being more marked on the left side. There was a right central facial weakness and some weakness of the right upper and lower extremities. The tendon reflexes were more active on the right, and a transient ankle clonus was demonstrable on the same side. The abdominal reflexes were sluggish, but equal. Skilled acts were poorly performed on the right side. Some rigidity and cogwheel movement and a tendency to forced grasping were noted in the right upper extremity.

Laboratory Data. The urine and blood tests were negative. The feces gave a four plus guaiac reaction. The cerebrospinal fluid was clear, colorless and free of cells. The initial pressure was 112 mm. of water. The Ayala index was 3.2. The vestibular tests were normal. X-ray examinations of the gastro-intestinal tract and chest were negative. An encephalogram showed bilateral internal hydrocephalus, and what appeared to be a mass in the anterior horn of the left lateral ventricle. It apparently compressed the foramen of Monro, producing lateral

* From the Neurological Service of Dr. Israel Strauss and the Laboratories.

displacement of the right lateral ventricle. It was estimated to be about 4 cm. in diameter. The third ventricle was also somewhat dilated and there was an impression on its left lateral and anterior surfaces. The aqueduct of Sylvius and the fourth ventricle appeared to be normal.

Course. The diagnosis of an expanding lesion in the left cerebral hemisphere, probably metastatic in origin, was agreed upon. No primary focus, however, could be discovered. During the performance of a Queckenstedt test (which was negative), compression of the jugular veins was followed by twitchings of the right hand and arm. These mild convulsive movements, of which the patient was not conscious, lasted about ten seconds. Subsequently the patient said that he believed that he was dreaming. He also recalled the frequent occurrence of such attacks during the past few months.

On January 30, a transfrontal craniotomy was performed. A flattened area was noted on the under surface of the left temporal lobe. The exploratory needle

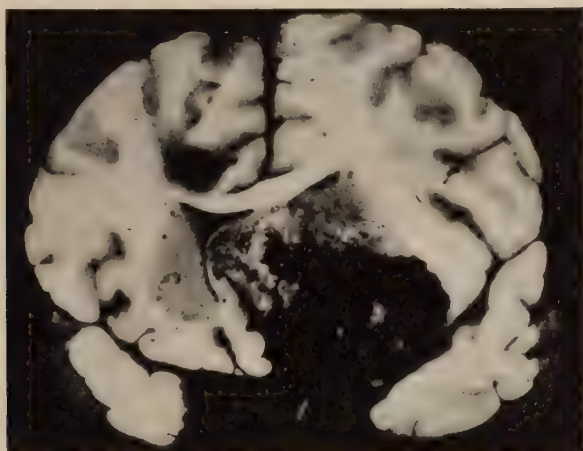


FIG. 1. (Case 1.) The appearance of the tumor invading the basal ganglions in the left cerebral hemisphere.

encountered resistance. By removing the overlying portion of the frontal lobe, a hard pink mass, measuring about 3 cm. in diameter, was disclosed. It gave the impression of being encapsulated. Large portions of the tumor were removed, and it was believed that the entire mass had been delivered. The patient ceased a few hours later without recovering consciousness.

Necropsy Findings. Gross Anatomy. The left cerebral hemisphere presented a shallow defect in the region of the orbital gyri, presumably the seat of the removed tumor. On sectioning of the brain, a large area of disorganization and discoloration was found in the left hemisphere (Fig. 1). It showed an eroded surface on its ventral aspect, which could be traced as far forward as the frontal pole. Posteriorly it could be traced back to the optic chiasm. The eroded area which was marked by brownish discoloration extended dorsally as far as a line going through the middle of the insula. Mesially it was bounded by yellowish tissue which occupied the septum pellucidum and displaced the latter toward the right. This

yellowish tissue gave the impression of neoplastic material which projected into the anterior horn of the right lateral ventricle. Tracing this tissue toward the left side, it could be found adherent to the undersurface of the corpus callosum and then passing into the basal ganglion on the left side. At this point it had narrowed the temporal horn considerably by the compression of the adjacent tissue and by direct invasion. It was quite likely that the disorganized tissue was badly dis-

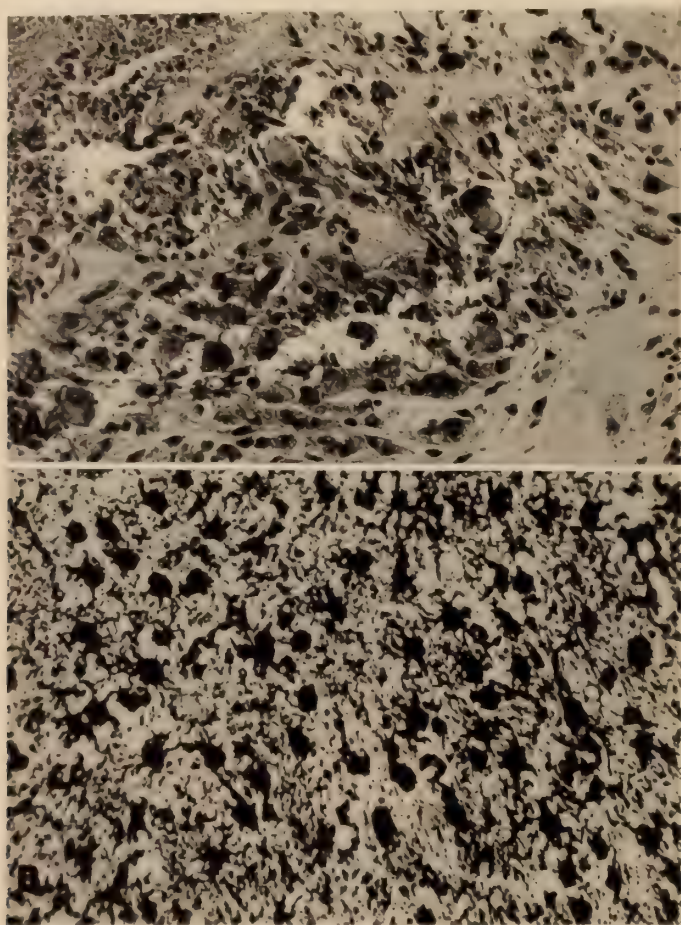


FIG. 2. (Case 1.) A. Tumor tissue showing the irregular arrangement and the variability in size and form of the tumor cells.

B. Tumor tissue showing the glial character of the tumor cells.

colored, hemorrhagic, tumor tissue which unquestionably was part of the residual tumor. In addition, there were several hemorrhagic areas in the left hemisphere which probably had occurred in the course of passing the aspiration needle. The hemisphere on the side of the tumor was markedly enlarged and edematous. The ventricular walls were colored with sanguineous fluid; this was particularly true of the left ventricle.

Microscopic Anatomy. The tumor tissue was largely necrotic and hemorrhagic. The tumor cells in the intact areas were arranged in a diffuse and chaotic fashion (Fig. 2A). There was a great assortment of cell types, some with small, round, deeply staining nuclei and abundant cytoplasm, some with spindle-shaped nuclei and cytoplasm streaming from either pole in fiber-like extensions, while many were of the giant multinucleated variety. Mitotic figures were common. Vessels were seen traversing necrotic areas, displaying marked endothelial proliferation and carrying along narrow zones of intact tumor tissue. A striking feature in one area was the presence of a number of large, irregular, patent and empty lacunae, lined by cells strongly suggesting ependyma. Silver stains applied to the tumor tissue revealed the presence of gliogenous elements (Fig. 2B) in all stages of differentiation, with a predominance of primitive spongioblastic and early astrocytic forms.

Comment by Dr. Globus. Of significance in this case was the rather rapid clinical course. This led to the suspicion that the lesion might be metastatic in character. However, the subsequent histopathological studies disclosed the gliogenous character of the tumor and gave ample explanation for the rapid course of a primary brain tumor. The tumor, having been identified as a spongioblastoma multiforme (1), which is often extremely rapid in growth, was in full accord with the clinical picture in this instance. Equally significant was the fact that, on X-ray examination, a mass was found protruding into the right lateral ventricle. Of course, there was no free tumor in the ventricle but the apparent protrusion of the tumor was most likely due to the peculiar distribution of air in a markedly reduced lateral ventricle. Another point of significance was the appearance of twitching in the right arm on carrying out the Queckenstedt test. This could best be explained by assuming that, on compression of the jugular veins, intracranial pressure was increased and the affected area of the brain was thus provoked to produce cortical discharges, unchecked by a striatum almost completely destroyed by the tumor.

Case 2. Spongioblastoma of the Left Cerebral Hemisphere. Dr. Mark Kanzer

History (Adm. 399297). A man, aged 56 years, was subject to occasional left occipital headaches for two years preceding his admission to the hospital (October 5, 1936). They had become increasingly severe and boring. On February 7, 1936, the patient slipped on an icy pavement and broke his right ankle. There was no head injury. He was confined to bed for three months. At the end of this time he was examined, found to be well and was told that his blood pressure was also normal.

His fatal illness began on July 1, 1936, when he experienced a feeling of "heaviness" in the right upper extremity. Two weeks later the right lower extremity became similarly involved and the right side of the face became flattened. When examined at this time, he was found to have hypertension with a systolic blood pressure of 200 mm. of mercury. In the course of the next three weeks the right hemiparesis became increasingly pronounced, so that the patient was unable to walk. His headaches, which previously had been intermittent, now became constant. For the two weeks preceding his admission, he was no longer able to speak coherently, became irritable and displayed other evidence of mental deterioration.

Examination. The patient was apathetic and disoriented. He had no insight into his condition and quickly lost interest in his surroundings. He showed a moderate anomia and was unable to formulate complete sentences. His voice

was hoarse, his speech was slow and scanning. There was marked perseveration. The patient frequently kept his left eye closed. When his eyes were open, the left palpebral fissure would become narrow. There was a slight enophthalmos of the left eye. The right pupil was larger than the left and reacted sluggishly to light; the left pupil was irregular in shape and did not respond at all to light. Both pupils reacted poorly in accommodation. There were a few nystagmoid jerks to the right. The corneal reflexes were diminished on both sides. There was an incomplete right homonymous visual field defect, more marked in the right eye. The fundi revealed arteriosclerotic vessels. There was a right supranuclear facial weakness, marked weakness of the right extremities and a right hemihypalgesia. The deep reflexes on the right side were more active than on the left. There were definite Babinski and Chaddock signs on the right side and questionable ones on the left side. The abdominal reflexes were diminished on the right. The blood pressure was 175 systolic and 105 diastolic.

Laboratory Data. The cerebrospinal fluid was clear, with an initial pressure of 200 mm. of water; it contained one mononuclear cell per cu. mm. The Ayala index was 4.2. The total protein content was 50 mg. per 100 c.c. The blood contained 16 mg. of urea nitrogen per 100 c.c. The red blood count was 5,000,000; the white blood count, 9,000 per cu. mm.; and the hemoglobin, 85 per cent. The blood Wassermann test was negative. A roentgenogram of the chest was negative. A roentgenogram of the skull revealed a defect in the right frontal bone near the coronal suture. Within this area there was a dense shadow which was thought to be a metallic body.

Course. The diagnoses considered were a cerebral neoplasm or a vascular lesion in the left frontoparietal area. The signs progressed, with an increasing loss of power in the right upper extremity. A repeated visual field examination again disclosed a right homonymous hemianopsia. The aphasia became more marked and was of a mixed type with motor disturbances predominant, making it impossible to carry out a complete mental status. On the sixth day in the hospital, he suddenly became stuporous. A craniotomy was then performed; it disclosed thrombosed vessels on the surface of the brain and an area of softening in the left frontoparietal region. The exploratory needle entered the ventricle and yielded 50 c.c. of clear fluid. At the close of the operation it was thought that the entire picture could be explained on the basis of a vascular disease. The patient remained in stupor and died on the following day.

Necropsy Findings. Gross Anatomy. The gyri of the brain were flattened, and there was a small hemorrhagic area, measuring about one centimeter in diameter, visible on the surface of the right frontal lobe. Both cerebral peduncles were elongated and thickened. The left peduncle was larger and measured one and one-half inches wide and two inches long. The optic chiasm and tracts were elongated. Both mammillary bodies were pushed to the right. On the lateral side of the left cerebral peduncle there was a reddened softened area, one-half inch by three-quarters of an inch. The pons was somewhat displaced and its left side was soft. The vessels comprising the circle of Willis were distorted and stretched, displaying a few atheromatous plaques.

On sectioning the brain, a large tumor was found in the left cerebral hemisphere. It extended anteriorly as far as a point one centimeter posterior to the genu of the corpus callosum, passed through the internal capsule and lenticular nucleus, spread-

ing, as it passed backward, so as to almost completely replace the thalamus and the adjacent lenticular nucleus (Fig. 3). Extending backward, it almost completely replaced the left side of the midbrain and could be followed into the pons. The tumor was very vascular and had the gross appearance of a spongioblastoma.

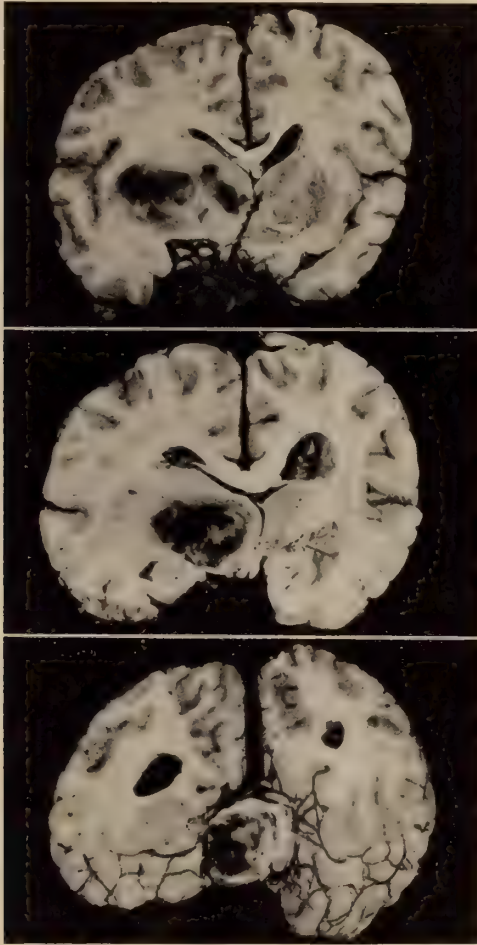


FIG. 3. (Case 2.) The tumor, maintaining a more or less deep-seated location, extends through almost the entire length of the left cerebral hemisphere as caudad as the midbrain.

Microscopic Anatomy. The tumor tissue was densely cellular and rich in blood vessels. The small arteries showed proliferation of the endothelium. Many of them were partially or completely thrombosed. There were extensive areas of hemorrhage containing deposits of pigment. The cells were predominantly glial in type. Many multinuclear and some cells, giant-like in type, were seen (Fig. 4). There were a few mitotic figures.

Comment by Dr. Globus. The rather brief history with the initial symptom of loss of power, rapidly developing into a right hemiplegia, with impairment of speech and mental changes, in the presence of moderate hypertension, made the diagnosis of brain tumor at first somewhat uncertain. The absence of papilledema and the presence of retinal arteriosclerosis made it difficult to exclude a vascular disease. However, the experience of this service with the so-called "acute brain tumor" (2), in view of the subsequent clinical course, led to an exploratory craniotomy. Even then, the diagnosis of brain tumor was not settled. The post mortem find-

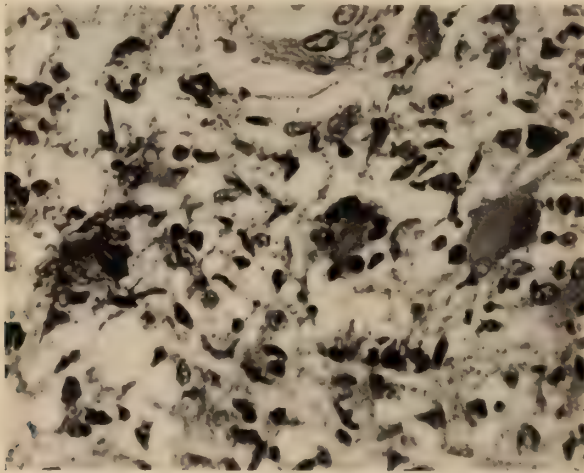


FIG. 4. (Case 2.) Tumor tissue showing multinucleated giant cells characteristic of spongioblastoma multiforme.

ings, however, disclosed the presence of an extensive, highly vascular, primary malignant tumor of the type termed spongioblastoma, which was a lesion fully in accord with the clinical picture presented in this case.

Case 3. Transitional Glioma of the Frontoparietal Lobe. Dr. Theodore Meltzer

History (Adm. 391625). The patient, a man 50 years of age, entered the hospital on April 4, 1936. He gave a history of excessive alcohol consumption and of a venereal infection contracted at the age of 30 years, for which he had not received any treatment. He was said to have been in good health until three months previous to his admission to the hospital, when, while bearing a heavy load, he noticed for the first time some weakness in his right hand and arm. This was followed soon after by a sensation of numbness in the right hand and by clumsiness which was evident on buttoning his shirt. Both the weakness and the numb feeling progressed rapidly so that he was soon not able to use the affected extremity. Several weeks later the right upper extremity began to display spontaneous movements, manifested by clenching and unclenching of his right hand and by convulsive flexion and adduction of the right arm. These attacks at first occurred at long intervals, but later became more and more frequent until they would recur several times a day. They would set in without warning, would last from five to ten minutes, and were followed by a feeling of tiredness and soreness in the muscles

of the affected extremity. The patient was conscious during these attacks and would remember all that took place during them. In the last few weeks the numbness, which previously had been confined to the right hand, spread to involve the whole arm. With this the patient lost the ability to tell the position of his hand and whether he was holding anything in it. During the week preceding his entry into the hospital his speech became indistinct. His voice became hoarse, but he was suffering from a head cold at that time. On the day before he entered the hospital he passed through a convulsive episode during which, for the first time, the right side of the face, as well as the arm, were involved.

Examination. The patient was well nourished and well developed. He had an unproductive, brassy cough. There was tenderness over the left parietotemporal region of the skull. His enunciation was poor; his speech, somewhat dysarthric; and his voice, hoarse. The left pupil was larger than the right; both reacted poorly to light, but well in accommodation. The nasal margin of the left disc showed some blurring and the retinal veins were somewhat engorged. The right corneal reflex was less active than the left. There was a right lower facial weakness. The pharyngeal reflexes were diminished. The biceps and radialis reflexes were more active on the right side. The knee jerks were obtained only upon reenforcement, the left readily so. The ankle jerks were absent. The abdominal reflexes were not elicited. There was a bilateral loss of plantar flexion, but no definite Babinski sign was elicited. Cutaneous sensibility in all modalities was reduced in the lower part of the face and the upper and lower extremities on the right side. Vibratory and position senses were absent in the right hand. There was weakness of the entire right upper extremity. Abarognosis and astereognosis were present in the right hand. Slight drifting of the outstretched right arm was noted. The finger-to-nose test was poorly carried out on the right side, and the ability to do skilled acts was markedly impaired on the same side. Tremor of the outstretched fingers of both hands was noted. Fibrillations, most pronounced in the hamstring muscles, were observed. The blood pressure was 140 systolic and 84 diastolic.

Laboratory Data. The cerebrospinal fluid was clear and under an initial pressure of 130 mm. of water. It contained 8 lymphocytes per cu. mm. The globulin and sugar values were within normal limits. The hemoglobin was 100 per cent; the red blood cell count, 4,200,000; and the white blood cells, 6,200, with 52 per cent polymorphonuclear neutrophils and 48 per cent lymphocytes. The blood Wassermann test and that of the cerebrospinal fluid were negative. A roentgenogram of the chest was negative.

Course. While in the hospital, Jacksonian seizures affecting the shoulder girdle and upper extremity on the right recurred. During these seizures the arm was alternately flexed and extended at the rate of about once every two seconds. Repeated visual field examinations revealed no abnormalities. A focal organic lesion in the left parietal region was considered. However, the prostate gland was found to be enlarged and increased in consistence and the question of multiple metastatic lesions was raised. A punch biopsy of the prostate, however, revealed no evidence of malignancy. In the meantime, the patient's dysarthria became more marked. A flaccid right-sided paralysis developed affecting both the upper and the lower extremities. There now developed emotional instability. In view of the new developments, a left parietal craniotomy was performed (May 18, 1936) and a fairly superficial neoplasm about 3 cm. in diameter was removed. The following day

the patient became drowsy and stuporous. The wound was reopened and some clotted blood was removed, following which the patient gradually became more alert. On the sixth postoperative day he again became unresponsive. A lumbar tap yielded xanthochromic fluid under a pressure of 320 mm. of water. The pulse rate dropped suddenly to 50 per minute. Bronchopneumonia developed and the patient died on the twelfth day after the craniotomy.

Necropsy Findings. Gross Anatomy. In the left parietal region there was a small hemorrhagic area, about 3 cm. in diameter, which was the site of the operation. The tissue around it, involving nearly the whole parietal lobe and the first temporal convolution was hard and nodular, and gave one the impression that there

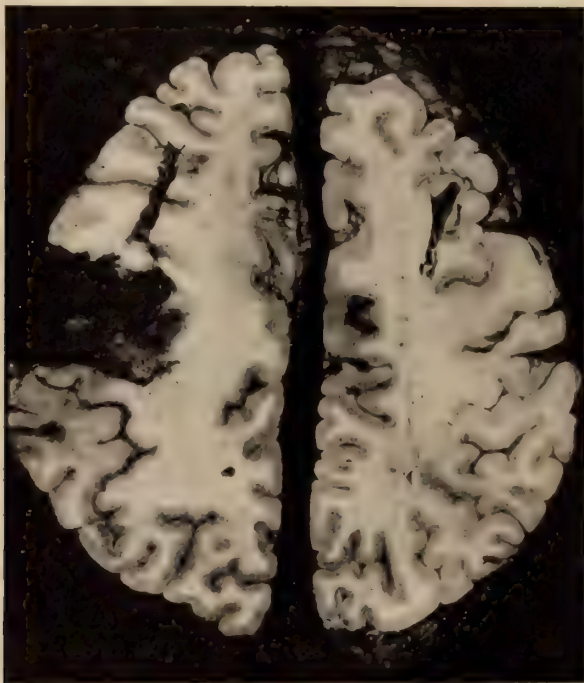


FIG. 5. (Case 3.) The tumor is vascular and occupies the left frontoparietal lobe

was a large subcortical mass. The left cerebellar tonsil was about twice the size of the right and had at its base a sharp encircling indentation, due to the pressure of the edge of the foramen magnum.

On sectioning of the brain, the left hemisphere was found to be enlarged and markedly edematous. In the region of the surgical field, which occupied the parietal lobe and extended forward so as to involve the postcentral gyrus completely and down as far as the Sylvian fissure, was a quadrilateral area of discoloration extending from the surface into the depth of the hemisphere for a distance of about 4 cm. (Fig. 5). This area was brownish red in color, apparently neoplastic, and was surrounded by a wide zone of edema. It seemed that the major portion of the tumor had been left unremoved.

Microscopic Anatomy. The cerebral cortex in the direct proximity to the area of discoloration showed complete loss of normal architecture, due to the presence of dense masses of cells, probably neoplastic in character (Fig. 6A). At points, there seemed to be a fusion between the similarly invaded meninges and the under-

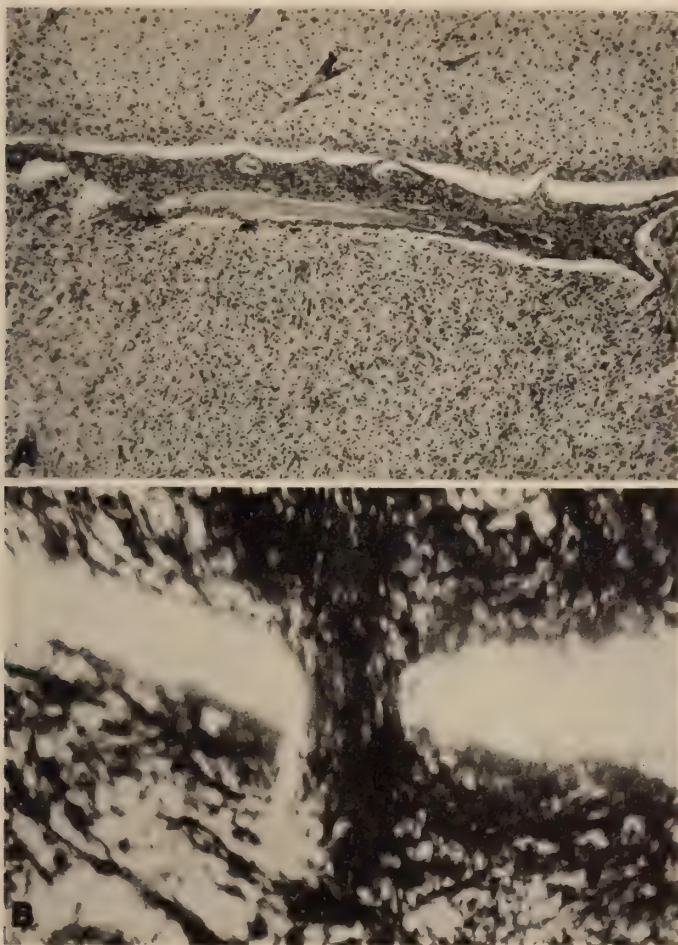


FIG. 6. (Case 3.) A. Tumor tissue, showing the complete loss of the normal cyto-architecture of the cortex, due to invasion by the tumor cells. Note the extension of the neoplastic elements into the meninges.

B. Glial fibers bridging over the subarachnoid space.

lying cerebral cortex. When studied with special stains, these cells within the invaded area of the cortex were found to be of glial derivation, displaying variations in size and contour and containing here and there mitotic figures. At several points narrow bands were seen bridging over the subarachnoid space (Fig. 6B). These bridges were found to contain argentophilic fibers which could be traced to

glia cells on either side of these bridges. The tissue in the neighborhood of the tumor contained many isolated atypical nerve cells of the type not unlike that found in tuberous sclerosis.

Comment by Dr. Globus. In this case again, the rather abrupt onset and the rapidity with which the symptoms developed led the service to suspect a metastatic lesion. This diagnosis, however, was soon dismissed and, since the objective signs permitted precise localization of the lesion, exploratory craniotomy was found advisable. This was undertaken not only for the purpose of identifying the lesion, but, in view of the presence of the hemiparesis, hemisensory symptoms and Jacksonian fits, it was felt that a tumor was present and might respond to surgery. However, the nature of the tumor was one which was similar in many respects to the spongioblastoma multiforme. It was described under the name of transitional glioma, but presented the invasive character and the tendency for rapid growth noted in the more malignant form of tumor. This, of course, explained the poor surgical results.

Case 4. Glioneuroma of the Right Frontoparietal Lobe. Dr. Theodore Meltzer

History (Adm. 392865). The patient was a 45 year old man who was perfectly well until two years and two months before admission. At that time, while driving an automobile, he felt a twitching of his toes and immediately thereafter became dizzy. He had no recollection of what took place after that, for the next thing he knew was that the car was at a standstill two blocks farther away and he was leaning over the wheel. Upon arriving home, he felt weak and dizzy. That night he had six convulsions, each lasting fifteen to twenty minutes. These were reported by the patient's wife to consist of generalized twitchings accompanied by frothing at the mouth, occasional biting of the tongue and complete loss of consciousness. Subsequently the attacks became milder but did not decrease in number. Although the attacks continued, after one year they were no longer accompanied by unconsciousness. The patient described the attacks as beginning in the left foot and spreading to involve the left side of the body. He stated that the episodes would last but a few minutes; and that excitement would in some instances be the precipitating factor. Since the accident the patient had been suffering from a loss of memory for recent events. He also became a little irritable and quarrelsome. One year before admission the patient was observed at another hospital where an encephalographic examination revealed a slight atrophy of the cerebral hemisphere. He received several injections of an arsenical preparation for possible central nervous system lues. During the year previous to admission to this hospital the patient noted that there gradually developed a considerable weakness of the left upper extremity followed by weakness of the left lower extremity. Six months before admission he noticed a peculiar tremor of the left hand and would find great difficulty in releasing his grasp on an object. Since the onset of the illness the patient had been suffering from headaches which had gradually diminished in intensity. At the time of admission they occurred daily and lasted about one hour.

Examination. The patient was well nourished. He was mildly euphoric and did not worry about his physical condition. The left palpebral fissure and the left pupil were larger than the right. Both pupils were slightly irregular in shape and reacted to light and in accommodation. The left disc showed temporal pallor.

Slight bilateral limitation of the external gaze was noted. There was a left central facial weakness. There was a left-sided hemiparesis with diminished abdominal reflexes and hyperactive deep reflexes. A Babinski sign was present on the same side. The left hand exhibited forced grasping. At the base of the right lung there were some râles.

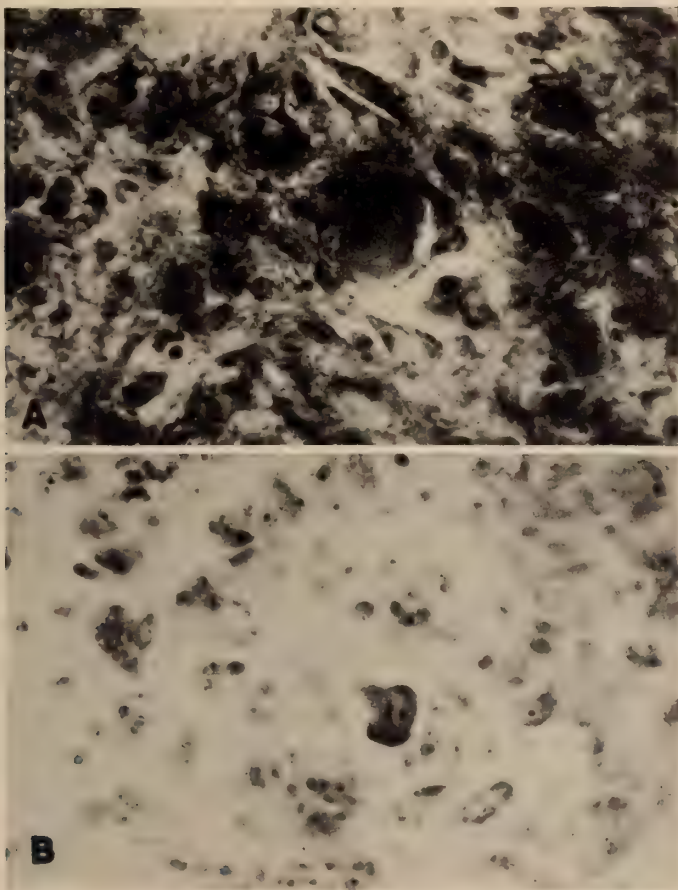


FIG. 7. (Case 4.) A. Tumor tissue showing large and irregularly shaped cells, alongside bipolar fusiform elements.

B. Tumor tissue showing nerve cells in various stages of ripening.

Laboratory Data. The blood showed a leucocytosis of 12,200 with 78 per cent polymorphonuclear leucocytes.

Course. The diagnosis of an expanding lesion in the right cerebral hemisphere, probably benign in nature, was made. Caloric tests gave normal responses. The visual fields were normal. An encephalogram showed marked depression of both lateral ventricles with obliteration of the subarachnoid channels on the right side. There was also a concavity in the body of the left lateral ventricle. Apart from a

few convulsive seizures, the status of the patient remained unchanged. Two weeks after admission to the hospital a craniotomy was performed and a tumor which occupied the right paracentral area was removed. Following the operation the patient remained drowsy and responded very little to stimulation. The temperature rose steadily and he died on the fourth postoperative day.

Necropsy Findings. Gross Anatomy. In the right parietal lobe, adjacent to the falx cerebri, there was a large defect in the brain substance. This was filled with clotted blood and macerated tissue. The operative site was discolored and hyperemic. Some clotted blood was present at the base. On sectioning of the brain, aside from some necrotic tissue lining the defect, there was practically no alteration of significance. No tumor tissue could be detected in the post mortem material.

Microscopic Anatomy. A biopsy of the tumor revealed it to have a very cellular pattern. The cells were scattered through densely woven glia fibers. The vessels were very numerous and were marked by endothelial proliferation. There were many small areas of perivascular hemorrhages. The cytoplasm in many cells was abundant and the nuclei were centrally and eccentrically placed. The cytoplasm of some was densely stained; of others, pale. They were usually irregular in outline, of all sizes and shapes, some extremely large (Fig. 7A), others were elongated and had cytoplasm with extensions at both poles. Many of the nuclei, especially the larger ones, had nucleoli and some had two nucleoli. One cell was seen undergoing mitotic cell division. There were multinuclear giant cells. Most of the cellular elements were fairly well differentiated, some approaching the form of mature astrocytes. On further study, particularly with the use of Nissl stains, the tumor was found to contain also many ripe and partially ripe nerve cells (Fig. 7B). Hence the diagnosis of a glioneuroma was made (3).

Comment by Dr. Globus. Of significance in this case are: the relatively long clinical course; the early occurrence of atypical Jacksonian attacks, followed by more generalized convulsive seizures; the subsequent change of the character of the convulsions with the return to the Jacksonian variety; the absence of localizing encephalographic findings in the early stages of the disease; and the subsequent development of peculiar cortical discharges affecting the patient's left grasp. Here the clinical manifestations seem to be in accord with the histologic character of the growth. The nature of the tumor was such as to provide the brain with a larger number of cells which, in turn, may have interfered with the normal function of the normal cells. It may thus be postulated that the normal functions were distorted and new functions, or the discharge of extraneous impulses, were added.

Case 5. Blastomatous Malformation of the Optic Chiasm and Optic Nerves.

Dr. Edward Weinstein

History (Adm. 393928). A woman, aged 42 years, gave a history of malaria at the age of 18 years, at which time she also had an hemoptysis. At the age of 24 she had noted the presence of two small nodules in her scalp. At the age of 32 years she again coughed up a cupful of blood in the course of what was believed to be a "chest cold". At the age of 37 she was said to have had a left frontal "sinusitis" for a period of one year.

She entered the hospital on June 1, 1936, complaining of diminution of vision in the left eye for a period of ten years. At times she could see only the superior

portion of an object and would have to lower her head to obtain a full view. During the last four years she became subject to severe occipital headaches, and, when reclining, she would experience a throbbing in her head. The field of vision of the left eye had gradually become smaller so that eight months before admission to the hospital she could see only a small patch on the nasal side and two months later she became completely blind in this eye. At about this time the patient was awakened one night by an excruciating pain in the same eye. It felt very hard and acquired a dull glassy appearance. Subsequently the eyeball grew prominent and became displaced,—at first, outwardly, and then upward. The eye showed a bluish discoloration in the morning. She also developed tinnitus in the left ear for two weeks preceding her admission.

Examination. The patient was well developed and well nourished. There were two small nodules in her scalp. She was emotionally disturbed, greatly worried over her condition and cried easily. The sense of smell was impaired on the left side. This may have been due to a nasal polyp which was present and reduced the nasal orifice. The left eyeball was markedly proptosed. The left malar and temporal regions were enlarged. Attempts to push the eyeball back into the orbit met with resistance. The left eye did not move fully laterally, inwards and downwards, but it was felt that this was due to the exophthalmos and not to a nerve paralysis. The left palpebral fissure was much wider than the right. Light perception in the left eye was almost completely lost. During the examination of the fundus the patient experienced severe pain in this eye. The left pupil was dilated, did not react directly to light, but reacted consensually to light and in accommodation. The right pupil, however, was normal. The left fundus showed a primary optic atrophy and a narrow ribbon of retinal edema with yellowish white exudate between the disc and the macula. The retina was thrown into folds, but was not detached. The only other positive finding was a decrease of the abdominal reflexes on the right side.

Laboratory Data. The cerebrospinal fluid was clear, under an initial pressure of 120 mm. of water, and contained three mononuclear cells per cu. mm. and 68 mg. of protein per 100 c.c. The blood and urine tests were negative. A roentgenogram of the skull revealed marked absorption of the greater wing of the sphenoid bone on the left side and an enlargement of the left optic foramen.

Course. The local eye findings and the roentgenographic evidence of a destructive lesion pointed to a diagnosis of a retrobulbar neoplasm on the left side. The probability was that of a meningioma of the sphenoid ridge, but a primary tumor of the optic nerve or chiasm was also considered. The presence of the two nodules in the scalp, of fifteen years' duration, also gave rise to the possibility of von Recklinghausen's disease affecting the optic nerve. Perimetric studies revealed, in addition to the amaurosis of the left eye, a diminution in the right temporal color field. While in the hospital, the patient experienced left-sided headaches on changing the position of her head. She noted that in the evening her left eyelid drooped, and this was confirmed on examination. Ten days after admission a left frontal craniotomy was performed and a grayish-red cystic structure, the size of a small chestnut and containing neoplastic tissue, was seen in the chiasmal region. During the operative procedure profuse hemorrhage was encountered, which was exceedingly difficult to control. The postoperative condition of the patient was poor. A

right hemiplegia developed and the patient sank into coma. The following day ligation of the left common carotid artery was performed, shortly after which the patient ceased.

Necropsy Findings. Gross Anatomy. The dura over both hemispheres had a bluish appearance, due to a considerable accumulation of blood in the subdural spaces. The left temporal and frontal lobes were badly macerated and soft. On reflecting the frontal lobes upward, the left optic nerve was found swollen irregularly. It was discolored, cystic, and seemed to be the seat of tumor formation. The optic chiasm was also swollen (Fig. 8), and was represented by a mass of brownish yellow tissue presenting small cystic areas at irregular points. The left sphenoidal ridge was eroded and friable, particularly near the left optic foramen. Within the orbital fossa the optic nerve mushroomed out into a fleshy swelling which affected its entire retrobulbar course. The left anterior and posterior clinoid proc-



FIG. 8. (Case 5.) The markedly swollen and distorted optic chiasm and optic nerves.

esses were absent. The right optic nerve was also swollen to about twice its normal size and apparently infiltrated by tumor tissue extending from the optic chiasm. There was a large subarachnoid effusion of blood over the ventral surface of the brain stem. There appeared to be a thinning of the floor of the third ventricle due to the upward pressure by the chiasmal mass. On sectioning, the optic chiasm and nerve were found to contain a central hemorrhage.

Microscopic Anatomy. Sections taken from the region of the prechiasmal optic segment, stained by various methods, revealed the following: -an unusually large number of blood vessels, showing hyalinizing alterations, assuming an aneurysmal formation, cirroid and others (Fig. 9). About these blood vessels there were large collections of cells, of which many were glia. There was marked demyelination with exposure of some axis cylinders (Fig. 10A) and accumulation of macrophages. Many cells which were neuroblastic in character were present (Fig. 10B). Glial fibers were also in abundance. Malformation in the optic chiasm, in which the

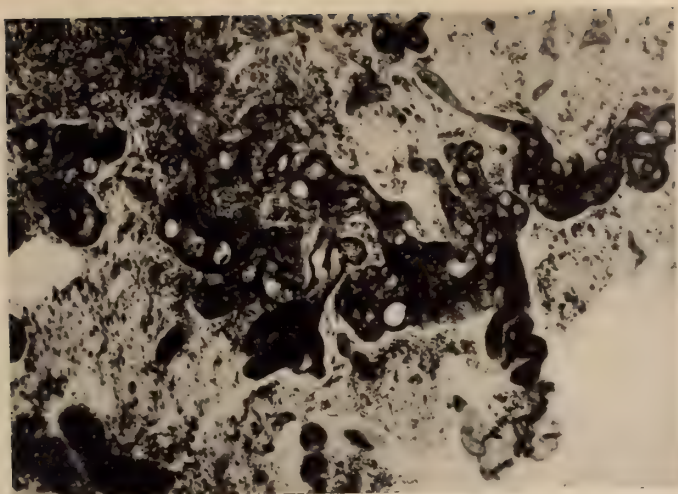


FIG. 9. (Case 5.) Tissue of the optic chiasm showing many irregularly dilated and tortuous vascular channels displaying hyalinizing walls.

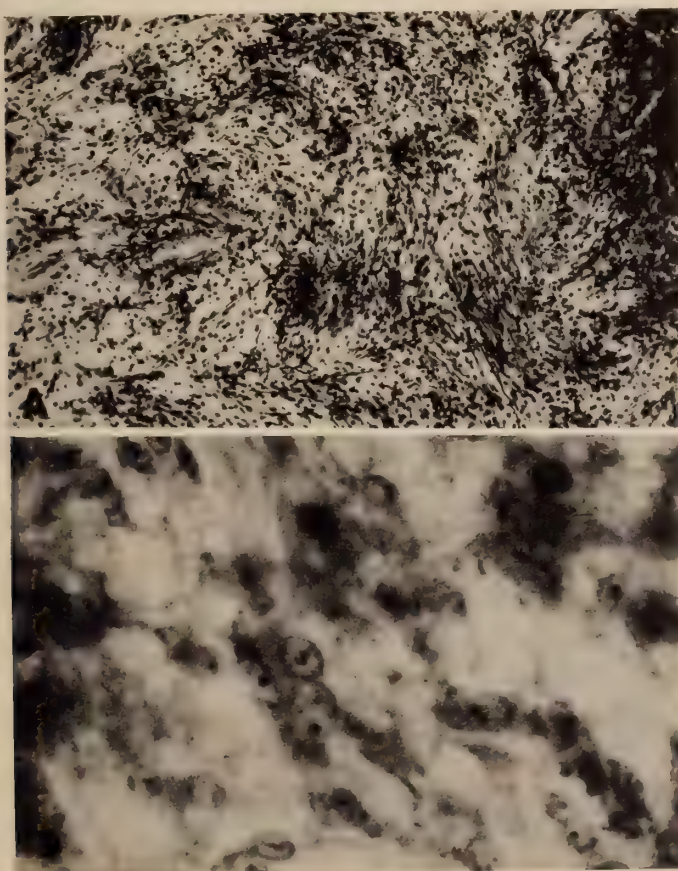


FIG. 10. (Case 5.) A. Demyelinated, naked optic fibers in the optic chiasm.
B. Poorly differentiated nerve cells in the tissue taken from the optic chiasm.

blood vessels were most likely the basic element, with the glia assuming a secondary character, was considered the most likely diagnosis. This condition is not unlike that described by Globus and Doshay (4) in connection with vascular alteration in the spinal cord.

Comment by Dr. Globus. This case presented exceedingly rare conditions. The long duration of the impairment of vision unquestionably pointed to the fact that the affliction of the optic nerves, while not of the extent found at post mortem, was nevertheless present at least ten years before the fatal issue, and most likely earlier. There was even a probability that the hemoptysis and the nodules in her scalp had some relationship to the character of the lesion, which was ultimately found in the optic chiasm. Indeed, the long duration of the lesion and the local manifestations justified the diagnosis of a meningeal tumor. But it was also significant that a primary tumor of the optic chiasm and the optic nerve were being considered. It was obvious, from the study of the tumor, that its removal was impossible, but it was equally true that the rarity of this form of neoplasm, the mixture of which was suspected, did not permit its uncontested recognition. The tumor showed itself to be a form of developmental anomaly, upon which neoplastic potencies were superimposed, and for this reason the term blastomatous malformation was adopted.

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PHYSICAL THERAPY IN THE MODERN HOSPITAL*

WILLIAM BIERMAN, M.D.

Modern surgery and pharmacology justify their existences not only on the basis of controlled clinical results but also on the objective observations made in numerous experiments. If physical therapy, the other member of the triad forming the foundation for our therapeutics of today, is to assume the corresponding position which it merits, it must also do so on similarly firm ground. At the present time the solid pillars of accurate facts extending to the rocky substratum of irrefutable truths are all too few in the grand mass of shifting sands of unproved assertions upon which physical therapy rests.

This division of therapeutics needs many more such concrete pillars. In general, the possibility of constructing them is nowhere as good as in the hospital. It is here that clinical changes are most carefully noted and recorded—and not by one but by many observers in the several medical fields. The determinations of change are made, not by the physical therapist who administers the treatment, but by the doctors of the service to which the patient belongs. The hospital likewise is the place where experiments are best conducted because the data to be investigated should be immediately applicable for the diagnosis or treatment of disease.

Fact-finding in physical therapy might well include the investigation of the physical and physiologic bases for the treatments which have been administered for many years in this field, and, in addition, the application of many new procedures. The discoveries in physics, in engineering, in electricity, and in the kindred sciences and technologies, present vast possibilities for medical usages. For proper assistance in this work, a hospital physicist is necessary. It is probable that the hospitals of the immediate future will consider the physicist as an individual whose importance in his own sphere is as great as the hospital chemist's is now considered to be in his.

The hospital presents the great advantage that it already contains the other laboratories and clinical divisions of medicine essential for research. Such determinations must necessarily represent the cooperative effort of

* This article and the other communications in this issue were presented by members of the department of physical therapy and of other divisions of the hospital on April 13th, 1938, at the Spring Meeting of the Eastern Section of the American Congress of Physical Therapy. The meeting was held at The Mount Sinai Hospital and marked the official opening of its enlarged and newly equipped department of physical therapy.

men in all fields of medicine and the allied sciences, and not merely the isolated activity of the individuals engaged in the investigation of the physical aspects of normal and of disturbed physiology.

The department of physical therapy should serve as a source for the dissemination of information. The physician today is not well informed in physical therapeutics. Only a small percentage have secured any teaching in this subject in their medical schools. The reading of books does not convey sufficiently exact ideas on technique. A didactic course is the most satisfactory method of securing such information, but such courses are unavailable for most. The physicians in the department of physical therapy must assume the rôle of teachers to the other members of the staff, even though they receive no monetary compensation for this. The technicians in the department should not be required to act as instructors to physicians outside the department. The physicians in the department of physical therapy do receive some measure of compensation for their teaching from the satisfaction of conveying information to those who desire it, and from the indirect clinical instruction secured by observing the medical reasoning applied by their fellow physicians in the diagnosis and treatment of diseases in the various specialties. This contact enables the physical therapist better to appreciate the relationship between his field in medicine and that of others. Such appreciation is necessary in order that the physical therapist may know the possibilities and limitations of the measures which he uses, in comparison with the others available. The opportunities for discussion of the therapeutic problems presenting themselves in the hospital make for better medical reasoning. Such discussions may well take place among the members of the department of physical therapy as well as among them and the physicians in other departments of the hospital.

There is also a great need for the teaching of physical therapy to undergraduate medical students. In addition to the didactic lectures, they should witness demonstrations of patients under treatment and of the techniques employed. This can be done in the wards and in the out-patient departments of the hospital, where post-graduate instruction should also be conducted. A third group who require the adequate teaching and training which only the facilities of a hospital can extend to them are the technicians who play so important a part in the actual administration of physical medicine. In addition to these educational activities, a properly organized department of physical therapy should continuously train a limited number of scientifically minded physical therapists among physicians who will practice in this field as a specialty and aid in its future development.

While most of the physical therapy treatments are administered to ambulatory patients, there are many who require hospitalization. Those too ill to go to out-patient departments or to doctors' offices frequently

cannot be adequately treated at home. Special treatments, such as physically induced fever (particularly if the temperature elevations are to be high and long maintained) should only be administered in hospitals. There are also treatments which require facilities and apparatus far too costly for the average private physician and which only the wider application of hospital practice can justify on an economic basis. Swimming pools, other hydrotherapeutic apparatus, and well-equipped gymnasia are beyond the financial capacity of the private practitioner.

Modern medical practice is beginning to pay attention to the individual who considers himself healthy, who has no specific complaints. For the maintenance of health, thought is being given to the subject of nutrition and to mental hygiene. This is as it should be; but there is another aspect to preventive medicine to which no specific attention is paid, and that is what I might call "physical hygiene," the application of physical activity designed to maintain the body at its maximum efficiency. During his school days—public school, high school, and college—it is considered essential that the student attend his gymnasium regularly. The granting of a diploma seems to indicate that not only has the individual passed through a definite educational process, but also that it is no longer necessary for him to pay any special attention to the further training of his muscles. The city-dweller may take himself to one of the gymnasia at a club or in a commercial organization. From neither one of these can we expect to issue valuable information as to the amount or character of the exercise necessary for the best health standards in a given group or in a given individual. With the rapidly increasing percentage of the middle aged and old aged persons in our population, the consideration of the proper exercise for health maintenance becomes a more pressing problem. The gymnasia in hospitals cannot be expected to meet this demand. However, it is there that the physician may develop different forms of exercise and a better appreciation of their effects in the normal as well as in the abnormal individual. They may thus set the pattern for others to follow.

Another consideration in the field of physical hygiene is the influence of climate. The study of the effects of variations in sunlight, of heat, of cold, of changes in barometric pressure, of moisture, of electrical charges in the atmosphere, is largely undeveloped. Obviously through the ages man has adapted himself to these changes in his environment. They play a part in the body's economy comparable in their importance to the chemical changes of food. When we understand them better, we will be able to prescribe them for the healthy and for the sick as we now do food and drugs. Such investigations along with others concerning the human body can best be conducted in the properly equipped hospital. Here the physical therapy department, if it is given the support which it deserves, may look forward to further expansion of its important activities in the years to come.

ULTRAVIOLET THERAPY ON A GENERAL SURGICAL SERVICE

RALPH COLP, M.D.

Not only have the domains of surgery been broadened by the annexation of fields formerly regarded as purely medical, but the operative mortality in all branches has steadily and progressively been diminished. These strides have been possible not only by the improvement in surgical technique and better asepsis, but by the closer cooperation of the specialists in internal medicine, pediatrics, neurology, endocrinology and physiotherapy. Surgeons have finally realized that the results in any branch of surgery are dependent to a large degree upon the adequate anteoperative preparation and meticulous postoperative care. This preoperative care encompasses a thorough cardiovascular survey, a complete urinary examination and an evaluation of the general physical condition of the patient. The cardiac, the hypertensive nephritic, the jaundiced, the obese, and the emaciated patient must be individually prepared before operative intervention can hopefully be undertaken in chronic conditions. We, as surgeons, have come to realize that the physical status in each individual case must be carefully evaluated and accurately judged, for the patient must never be fitted into a preconceived operative procedure, but rather the operation must be fitted to the needs of the patient. Multiple stage procedures in selected cases are never to be considered a reflection upon the technical ability of a surgeon. They are rather an index of his surgical judgment.

The postoperative period always requires accurate observation, because not only must fluid balances be maintained along definite lines, but the various untoward and seemingly unavoidable complications such as distention, pneumonia, thrombosis and embolism, must be energetically treated.

I believe that there is no group of patients who require more preoperative care and attention than those who suffer from chronic gastroduodenal ulceration, non-specific granuloma of the small and large intestine, ulcerative colitis, and the malignancies which may affect any part of the gastroduodenal tract. The majority of these patients, whether suffering either from inflammatory lesions or malignancies affecting the small or large bowel, not only show the effects of malnutrition reflected in weight loss and absence of tissue tonus dependent upon a deranged digestion and defective absorption, but also the chronic ulceration of the pathological lesions invariably results in a severe secondary anemia with all that it implies. Patients comprising this particular group when recruited from the slums of a large metropolitan area are grave operative risks. They are invariably inade-

quately and poorly fed and usually live under crowded conditions in poorly ventilated rooms. They are particularly apt to shun whatever little sunshine there may be during the winter months in order to avoid the rigors of the weather because of either insufficient clothing or because the derangement of the physical economy has made it impossible to keep warm. These statements are not made to dramatize a social situation but they are made to emphasize a fundamental fact that any patient confined to his room for weeks or months is apt to show the physical loss of the benefits of the actinic rays of the sun which, together with certain vitamins, seem essential for bodily health and tissue tone. We all know that operative wounds in poorly nourished, emaciated and anemic patients heal poorly, and that patients suffering from carcinoma of any organ, bleeding fibroids of the uterus and chronic gall bladder disease complicated by jaundice, are more apt to disrupt their wounds and eviscerate than other types undergoing operation. It is especially interesting to note that *Sokolow* of Leningrad in his paper on postoperative wound disruption and evisceration, in which he collected seven hundred and thirty cases from all parts of the globe, came to the conclusion that the time of the year had a distinct influence on the incidence of wound disruption. This was especially true in the Northern longitudes in which the period of winter is particularly long and the peasants are apt to remain indoors and eat canned goods with a complete absence of fresh vegetables. He found that December to June accounted for almost 70 per cent of wound dehiscences. This is more than a coincidence.

In a community such as New York City these physical geographic factors are not comparable to those Scandinavian countries and Northern Russia, but I feel sure that the absence of proper diet and sunshine, along with the underlying pathology, are instrumental in causing a general atony of all tissue. Even after a patient suffering from a chronic illness enters a hospital, his new environment, coupled with sleepless nights, loss of appetite, improper diet often necessitated by prolonged diagnostic procedures, plus the physical and mental trauma, incident to a ward existence, individually and collectively leave indelible imprints upon the nervous and metabolic system of the body. With these factors closely borne in mind, it is not difficult to see why wound dehiscences still exist, in spite of improvements in operative technique.

In 1933, I reviewed 2,750 consecutive laparotomies from the surgical and gynecological ward services of The Mount Sinai Hospital and found that wound dehiscence occurred in .9 per cent of the cases. As I reviewed these cases, certain conclusions became quite evident. The type of incision, the magnitude of the operation, and method and technique of wound closure, wound drainage or infection, bore little or no relationship to the frequency of dehiscence. While no disease affecting the peritoneum or its contents was free of this complication, it seemed to occur in those maladies characterized by chronic toxemia and accompanied by anemia, cachexia,

weakness and general debility. The crux of the problem seemed to rest in the failure of regenerative powers of the tissue to promote firm healing. It seemed that wound dehiscences would always be a surgical complication until means were at hand which would unfailingly promote the prompt healing of tissue in these specific cases.

I could not help but feel that the point which Sokolow emphasized, namely the absence of the sun, had not received sufficient attention. I felt that ultraviolet therapy should become part and parcel of the anteoperative preparation of some patients. Therefore, since July 1, 1934, in addition to the usual careful preoperative preparation of cases, I have been fortunate in securing the additional cooperation of the Department of Physiotherapy under Dr. William Bierman, in attempting to improve the physical status of those gastric and colon cases prior to operation. A group of physical therapists, such as is gathered here, needs no surgeon to tell them about the benefits derived from ultraviolet therapy. But there is more than the physical betterment; there is the psychological improvement in the morale of these patients which is nothing short of remarkable. All patients admitted to the surgical wards and requiring major surgery are given ultraviolet therapy routinely. Those who are able to walk, go to the Physiotherapy Department three or four times a week for treatment, and for bed cases, the lamp is brought into the wards. After a few treatments, they get the usual sunburn, and with it a feeling of improvement. Their looks become deceiving because their deadly, ashen white is gone, and the favorable comments elicited by relatives and friends on subsequent visiting days as to the improvement in their physical appearance does much to bolster their morale. I must agree with Mary Baker Eddy that the "will to do is half the cure," and any improvement in the morale is a battle won. The time is too short to present any statistics but I feel quite definitely that since the institution of ultraviolet therapy anteoperatively and postoperatively, the postoperative course of these patients, especially as concerns wound healing, has been materially improved. Ultraviolet therapy has proved a great help to the general surgeon in the anteoperative preparation and convalescence of his patients. Its use, however, in surgery, has spread to the operating room.

Dr. Deryl Hart, Professor of Surgery at Duke University, has employed the ultraviolet ray lamp while operating and he is most enthusiastic with the improvements in asepsis which he has obtained. He feels that since surgery has embraced operative procedures of greater magnitude and with inevitable trauma, the air-borne organisms have become a distinct hazard. The concentration of operative work by the increased utilization of operating rooms has added to the danger of infection from air-borne organisms. It is his opinion that many of the operative wound infections with staphylococci, which heretofore have been ascribed to contamination of the skin, are air-borne. In spite of all the precautions taken—masking, adequate

skin protection, changing of knives and the like—there has been but a small reduction in the number of infections. But recently these have been eliminated by sterilizing the air of the operating room with tubes emanating special anti-bacterial radiation. Undoubtedly these observations of Dr. Hart are of great importance, and in all probability no operating rooms will be equipped without special ultraviolet ray lamps in the future.

Upon the advice and stimulation of Dr. Bierman, we have also extended ultraviolet therapy to superficial wound and deep sinus infections through the use of the Quartz rod, and have used it in erysipelas with very gratifying results. We will grant that it is difficult to evaluate any treatment in erysipelas. The various therapies employed in this distressing and fatal complication have been legion. Each camp has its protagonists; each claims unusual results. The technique outlined by Dr. Bierman and Dr. Levenson is simple and they have kindly given me their routine and their results.

In the treatment of erysipelas, the mercury quartz ultraviolet lamp is applied as early as possible. A dose corresponding to several times that producing an erythema is applied. The distance and time employed varies with the efficiency of the burner. In general the radiation is permitted to shine from ten to fifteen minutes, with the burner held at a distance of about fifteen to twenty inches. The area irradiated includes not only the entire region of the lesion but also about one inch of the surrounding normal appearing skin. The ultraviolet radiation is followed by phototherapy from a carbon filament lamp. This is held at a distance sufficient to give the sensation of comfortable warmth. It is applied continuously until the decline in temperature and the fading of the lesion indicates the disappearance of the erysipelas. Only when the involvement spreads is the ultraviolet radiation repeated. There were sixty-four erysipelas cases treated at this hospital with this technique. Of this group, three patients died:—one was a nine month old child, who died of pneumonia; the second was a 44 year old man, who died of ulcerative colitis, although the erysipelas had cleared; and the third was a 40 year old man who had a sinus thrombosis and a positive blood culture. The remainder of these patients, in addition to four others with erysipeloid lesions who were treated by phototherapy alone, have recovered.

From this rather brief account, it is quite evident that the cooperation of the Department of Physiotherapy has become quite essential to a general surgical service, and that ultraviolet therapy has proved of great value as a weapon in the general armamentarium of surgeons in their battle for better operative results.

INDEPENDENT REGULATION OF CIRCULATION IN SKIN AND MUSCLES OF THE LOWER EXTREMITIES

SAMUEL SILBERT, M.D.

It has generally been assumed that when the circulation in the skin of the feet is increased by a therapeutic procedure a parallel increase takes place in the circulation of the muscles of the extremity. Such an assumption is apparent in the papers which report the effect of operations upon the sympathetic nervous system. Following ganglionectomy, a striking increase in the surface temperature of the skin of the feet has been noted by all observers, and this increased temperature has been accepted as evidence of increased circulation. The earlier reports of clinical improvement following this procedure stated that not only was pain promptly relieved and ulcers rapidly healed, but that intermittent claudication was also benefited (1, 2, 3, 4). Since intermittent claudication is due to a deficiency of circulation to the muscles, this clinical observation appeared to indicate that ganglionectomy resulted in an increase in circulation not only in the skin, but also in the muscles. However, as observations upon the clinical effect of ganglionectomy increased, it became apparent that earlier reports were incorrect and that intermittent claudication was little, if at all, benefited by this procedure (5, 6, 7, 8, 9).

It was the failure of sympathetic paralysis to relieve intermittent claudication that particularly excited our interest. It is possible to produce a satisfactory paralysis of the sympathetic nervous system for clinical purposes by means of a paravertebral injection of alcohol. The technique is simple and has been described by Labat (10). Thirty ambulant patients were treated by this method, in order to study the clinical results of such sympathetic paralysis. It was soon apparent that the circulation in the skin of the extremities could be increased by this procedure, but it was also regularly noted that the ability to walk was not improved. This clinical observation appeared to indicate that the circulation of the muscles was *not* increased by sympathetic paralysis.

In order to explain this fact and evaluate its significance, a group of us (11) decided to investigate the manner in which the circulation in the muscles of the lower extremities is regulated. It is well known that the blood flow in the extremities can be influenced by various procedures. Our object was to discover if the changes observed occurred simultaneously in both the skin and underlying muscles, and in what manner these changes were related.

It is generally accepted that variations in the temperature of the tissues

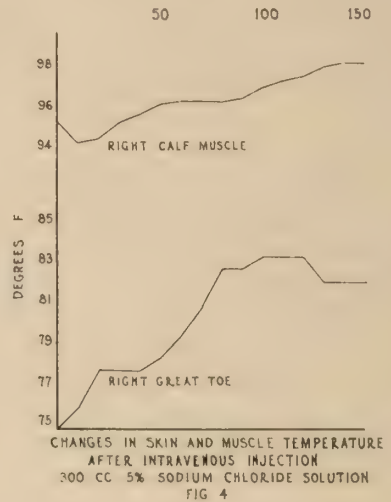
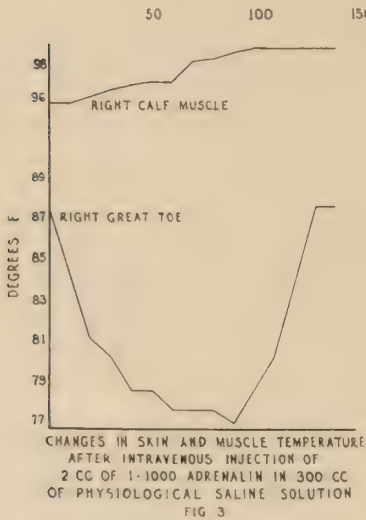
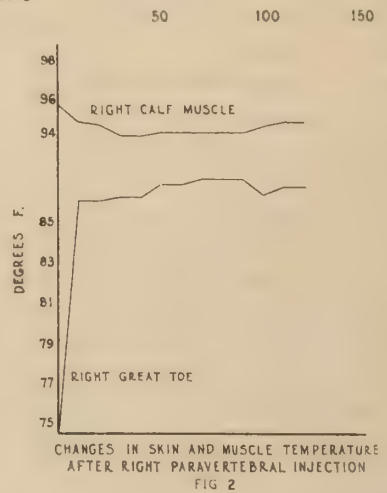
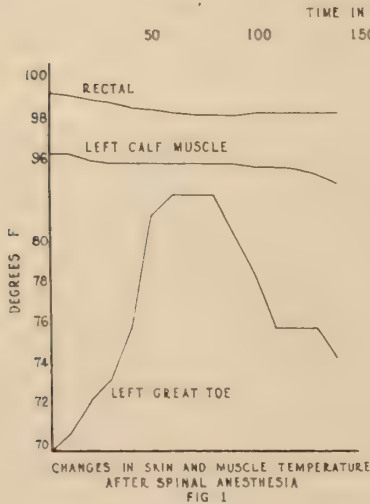
of the extremities are an indication of variations in blood flow. To study these changes independently thermocouples were used to determine skin surface temperatures and the temperatures of the muscles. Associated changes in body temperature were noted by means of a continuously registering rectal thermometer. In each experiment stabilization of skin, muscle and room temperatures was established before any procedure was begun. Temperature observations were continued for a period of from two to five hours in each instance.

From these studies it was at once apparent that changes in the temperature of the superficial and deep tissues of the extremities did not take place simultaneously. Immersing the upper extremities in water at a temperature of 45°C. for half an hour (Landis test (12)) resulted in elevation in the surface temperature of the skin of the feet, but the muscle temperature of the legs remained unchanged. By means of spinal anesthesia, complete motor, sensory and vasomotor paralysis was produced in the lower extremities. Following this procedure the calf muscle temperature remained unchanged, while the temperature of the surface of the skin became markedly elevated (Figure 1). Paravertebral injections of alcohol, which produce a prolonged paralysis of the sympathetic nervous system, to the lower extremities also failed to cause any elevation in calf muscle temperature although the skin surface temperature rose (Figure 2). As a result of these observations it appeared that paralysis of the nervous mechanism to the lower extremities causes no obvious change in the circulation of the leg muscles. The failure of ganglionectomy and paravertebral injections of alcohol to relieve intermittent claudication may thus be explained.

A study of the effects of intravenous injections of certain substances revealed other interesting changes. When 2 c.c. of adrenalin was given intravenously in 300 c.c. of physiological salt solution, a prompt and decided fall in skin surface temperature resulted from vasoconstriction, while the muscle temperature showed an equally prompt and decided rise (Figure 3). This observation indicated that injection of adrenalin increases the circulation in the muscles of the extremities at the same time as it diminishes the circulation in the skin.

Intravenous injection of 300 c.c. of hypertonic salt solution was regularly followed by elevation of both skin and muscle temperature (Figure 4). Continuous observations of the rectal temperature during and for several hours after such intravenous injections showed very slight rise (0.2 to 0.5 degrees Fahrenheit) or no rise in body temperature. The mechanism by which this increased circulation in skin and muscles is obtained is not yet clear. Patients with peripheral vascular disease treated with intravenous injections of hypertonic salt solution regularly show improvement in walking (13). The demonstration that such injections cause an elevation in the temperature of the muscles adds experimental evidence to substantiate

the value of this method of treatment. From the limited number of forms of treatment that we have studied thus far it is the only method which appears to increase the circulation in both skin and muscles.



FIGS. 1-4

The major problem in the treatment of patients with peripheral vascular disease is the relief of intermittent claudication. Practically all patients with circulatory deficiency present this symptom, and in more than half of them this is the only serious complaint. To relieve it, therapeutic procedures must be devised that will increase the circulation in the muscles.

On the other hand when ulceration is present, a method of treatment is desirable which will increase the circulation in the skin.

The evidence presented is sufficient to indicate that the circulatory response to therapeutic procedures is not necessarily parallel in the superficial and deep structures. It is no longer justifiable to conclude that an evident increase in the circulation in the skin is accompanied by a similar increase in underlying muscles. In the future each method of treatment must be studied to determine to what extent it independently affects the circulation of the muscles and of the skin. It will then be possible for the clinician to utilize that method which will answer his specific need.

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ARTIFICIAL HYPERPYREXIA IN THE TREATMENT OF ACHALASIA OF THE CARDIA (CARDIOSPASM)

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The application of physical therapy to various gastro-intestinal affections opens up a wide field of investigation. In this brief presentation we shall limit our discussion to the physical therapy of cardiospasm or so-called achalasia of the cardia.

Cardiospasm is essentially a chronic disease characterized by dilatation and inflammation of the esophagus, failure of the cardia to open (achalasia), and regurgitation. The chief theories advanced to explain its etiology are (1) psychogenic (Winkelstein), (2) inflammation of Auerbach's plexus at the cardia (Hurst), and (3) reflex (Larimore). In the therapy of the advanced stage of the disease, dilatation of the cardia seems to help most. Forceful methods are dangerous. The soft, mercury-weighted tube of Hurst is useful, but it frequently fails.

Martha Brunner-Ornstein of Vienna has enthusiastically advocated local diathermia to the cardia. She uses an esophageal bougie with an electrode at the end enclosed in a semi-permeable membrane which may be distended with normal saline. The dispersive electrodes are placed on the anterior and posterior chest walls, so that the diathermy current is concentrated at the cardia. Our experience with this method has been confined to one case which was treated by Dr. Brunner-Ornstein under our observation in the hospital. While there was some temporary improvement during three treatments, the patient's symptoms recurred rapidly.

Reasoning that the local elevation of temperature induced by this method is helpful to the inflammation and spasm presumably present, the idea occurred to one of the authors (W. B.) that general elevation of the body temperature by artificial hyperpyrexia may be at least as efficacious and, of course, less dangerous.

Accordingly, four patients with cardiospasm were treated with artificial hyperpyrexia. They received six to eight treatments, one every other day for two to three hours, with an elevation of the body temperature to 102-103°F. by rectum.

ILLUSTRATIVE CASES

Case 1. (Adm. 379738). H. S., male, 32 years old, with five years of cardiospasm. Not relieved by the mercury-weighted tube. Regurgitated food eaten two days previously. After six hyperpyrexia treatments,

regurgitation ceased, he gained weight, and the esophagus emptied the barium meal at once. Several weeks later, he was still comfortable. The esophagus then took fifteen minutes to empty the barium meal.

Case 2. (Adm. 339682). W. N., male, 22 years old, with eight years of cardiospasm. He had been treated for several years with the mercury-weighted tube. This is the patient who was treated with the Brunner-Ornstein tube with immediate recurrence of symptoms. After the hyperpyrexia treatments, his symptoms were unchanged but the emptying time of his esophagus improved from six hours to one and a half hours.

Case 3. (Adm. 377704). A. D., colored boy of 14. Severe cardiospasm for three months. Somewhat relieved by the mercury-weighted tube. Then his symptoms recurred and he was treated with hyperpyrexia. He experienced great relief. The emptying time of the esophagus was reduced to two hours from twenty-four hours.

Case 4. (Adm. 376775). A. C., male, aged 45, with a twenty-year history. The mercury-weighted tube could not be passed through his cardia. The usual medical measures failed. He was then treated with hyperpyrexia with great subjective improvement. He refused to cooperate in the radiographic studies.

COMMENT

It is, of course, apparent that the series treated is too small to permit of definite conclusions. The impression is gained, however, that these patients, refractory to other methods of therapy, have been helped by hyperpyrexia. The treatments did not cause any inconvenience since the patients were treated in an ambulatory fashion. There is practically no risk in this method, whereas the use of any type of mechanical dilatation harbors an element of danger.

These cases are presented without any claims for complete therapeutic success but rather as a new approach to a difficult therapeutic problem.

It is our plan to study accurately with a standard barium meal, after preliminary aspiration, the emptying time of the esophagus before using these therapeutic measures again. The patient will first be treated with the mercury-weighted tube, then with the Brunner-Ornstein local diathermy, and, finally, with artificial hyperpyrexia. A comparison of the results from the three methods, with reference to the subjective improvement and the emptying time of the esophagus, will be made. The tone of the cardiac sphincter during and after the hyperpyrexia treatments will also be investigated. In one case, studied by Dr. Henry Doubilet, the tone of the cardiac sphincter was considerably reduced during hyperpyrexia treatment.

SKIN REACTIONS IV

IONTOPHORESIS OF ALLERGENS AND HISTAMINE

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[From the Medical Service of Dr. George Baehr and the Laboratories]

A new way of studying allergic skin reactions may develop from recent experiments on the electrical introduction of the extracts of ragweed pollen into the human skin. In the ordinary course of events, the person with hay fever who is sensitive to the pollen of ragweed or of timothy grass, presents himself to the doctor for examination of his skin hypersensitivity. The doctor either scratches the skin and rubs a little bit of pollen powder into the wound formed, or he injects directly into the skin the extract of the pollen concerned. The same method is used in searching for sensitiveness to other allergens. These conventional procedures are useful, and at present constitute the formal method of approach to the study of the allergic patient. It would be of great advantage in the study of the allergic patient if tests could be made by placing the allergenic material directly on the *unbroken* skin.

The advantages of using a method in which the skin is left intact are those connected with the elimination of obscurity produced by tissue injury, and the advisability of having a minute amount of the powerful allergenic material introduced at a very slow rate at the same skin level. It has now been found that active constituents of extracts of ragweed pollen which have been dialyzed to remove substances of low molecular weight can be driven electrically into the skin by the phenomenon of electrophoresis. Electrophoresis is the movement of a charged particle in an electrical field. It had been noted in previous experiments with dialyzed ragweed extract that there was a skin reactive constituent which was negatively charged (when adsorbed onto quartz) at the acidity of the body fluids. It was therefore attempted to elicit allergic wheals by electrically driving these negatively charged ragweed ions from absorbent cotton into the skin of individuals sensitive to aqueous extracts of ragweed pollen. It was discovered that marked reactions were obtained after this electrical treatment for five to ten minutes, with currents so low as to be almost imperceptible to the patient. Whealing was observed in suitable subjects, that is, those sensitive to pollen extracts by injection. But the same technique employed on subjects not hypersensitive to ragweed did not result in a whealing reaction. In its present stage of development the method is not as sensitive as the intradermal method, but it is probably possible to increase its sensitiveness.

An effect of scientific rather than of practical interest, and as yet not quite understood, was that produced by the positive pole. Since the ragweed constituent was apparently negatively charged, it was not expected that the positive pole would elicit the skin reaction. Actually, the positive electrode was equally effective, if not more so, in electrically driving the ragweed constituent into the skin. It may be recalled that the pores of the skin have exactly the same kind of electric charges described for surfaces of blood cells, bacteria, and proteins in general. Whereas the electrical charge of blood cells or of ragweed extract enables the electrical field to move particles like these through a liquid, the electrical charge on the surfaces of the pores of the skin causes the liquid molecules in the pores to be oppositely charged. Since the skin itself cannot move when the electrical field is applied, the oppositely charged liquid molecules move. This movement of the liquid, well known as electroosmosis, carries substances suspended in it in the same way that a flowing river carries inert logs. In other words, the electroosmotic flow may carry passively anything that happens to be suspended or dissolved in it. It is perhaps by this electroosmotic flow that the positive pole may be effective.

Another force at work which has not been considered in detail is thermal diffusion over short distances. It has been shown by my associate, Dr. Gorin, that comparatively tremendous velocities are attained; for example, velocities as high as 0.03 cm. per second can occur. Since the sensitized tissues in the blood capillaries are directly beneath the uppermost layer of the skin, at a distance let us say of 0.1 mm., the diffusion process superimposed upon the electroosmosis of the liquid may well be an added factor.

Although the method of eliciting skin reactions to allergens by electrophoresis is still experimental, a rather wide field of investigation is opened up. There are innumerable substances which would be of interest to study: -the pollens of the trees, other grasses, dusts and other inhalants, such as danders, perfumes, etc. as well as foods. In addition it would be very important to ascertain if certain substances which are used in patch testing would give accelerated reactions or different reactions if introduced by electrophoresis. The positive patch test ordinarily takes twenty-four hours or more to appear. The substance is placed directly on the skin and a piece of gauze held in place by adhesive plaster covers the area. Perhaps if the substance were driven in by electrophoresis a simplified technique for the study of external irritants might be developed.

IONTOPHORESIS OF HISTAMINE

The local administration of histamine by iontophoresis has become increasingly useful. The galvanic method of introducing drugs into the skin has its analogy in the intravenous drip. When the intravenous drip is employed a very small quantity of the active pharmacologic substance is introduced extremely slowly so that good distribution in the blood stream

is obtained, without the trauma and injury produced by the rapid administration of a potent drug. And the electrical current similarly drives histamine into the skin. For if a sufficiently low current density is used, there is, practically speaking, no local tissue injury. With current densities of one-half milliampere, aside from a slight erythema due to the current itself, the tissue injury can be considered quite negligible. The local effects, then, are all due to the pharmacologic effects of the histamine which is administered very slowly. What does histamine do to the interstitial tissues and the skin in general when it produces its characteristic whealing effect? What are the mechanisms by which pain is relieved, swelling about arthritic points is reduced, and the temperature is raised in vaso-spastic conditions? A partial answer to this query may be found in recent experiments with Mrs. Engel, which were designed to study the absorption of dyes and of blood from the normal human skin. Dyes like bromthymol blue and trypan blue were injected intradermally, and the effects of histamine whealing at the site of the dye depot was observed. Whereas intradermally injected dyes may remain at the skin site for comparatively long periods, if a histamine wheal is produced with a suitable concentration of histamine, there is a marked acceleration of absorption. This acceleration of absorption can be explained in the following way: as the blood capillaries dilate, and blood plasma is transferred, through the blood capillaries into the interstitial tissues, there is not alone a dilution of the dye in the tissue, but also an acceleration of lymphatic absorption. So two factors operate: (1) the dilution of the dyestuff; (2) the acceleration of absorption. This acceleration of absorption was invariably observed. Perhaps a more striking example of the way in which histamine whealing produces accelerated absorption is the effect of histamine whealing on whole blood injected intradermally, or upon bruises produced either by venipuncture, or around the eye by accidental trauma. In the case of blood injected directly, it can be readily shown that most of the blood is removed after several treatments with histamine, within thirty-six hours, and frequently sooner; whereas if no histamine had been administered the bruise marks might have remained for more than a week. In experiments performed recently with Dr. Alice R. Bernheim of New York Hospital, the effects of Mecholyl and histamine on absorption were compared. It was found that an intradermally injected deposit of blood disappeared within twelve hours after treatment with histamine, but no effect whatsoever was observed with Mecholyl.

Similar experiments showed that absorption of dyestuffs was also not accelerated by Mecholyl, whereas the usual acceleration was always obtained by means of histamine. When treating hemorrhages about the eye with histamine, not alone is a good deal of the purple pigment removed, but also much of the tension is relieved after the swelling due to the histamine has disappeared. Rather large amounts of histamine can be given around the eye without any effect locally which might produce discomfort

to the patient. A patient with scleroderma received histamine about the lower eye-lid once daily for two weeks. The concentration of histamine was about 1:500, and the current density about one-half milliamperere. There were no untoward effects due to the administration of the drug. Nor have I ever observed any unpleasant effects after administration of histamine for hemorrhages in the tissues about the eyes.

To *summarize*, then, it seems that one of the most important and fundamental properties of the whealing process by histamine (or by allergens) is that there is a transudation of plasma, and acceleration of absorption, not alone of small molecules of the size of dyestuffs, but also of blood and blood pigment. Stated in another way, it can be said that the whealing process produces an irrigation of the connective tissues. One forces fluid, so to speak, into the tissues under increased pressure. The lymphatic drain increases and unquestionably removes toxic molecules which are not attached irreversibly to the tissues in question. Galvanic therapy, by means of histamine, therefore, is a non-injurious method of flushing the tissues with a new supply of plasma, repeatedly if necessary.

In the case of scleroderma which was treated by histamine, the tissues about the sclerodermatous patches remained soft for weeks. The patient felt that his normal facial expression was returning. It will be of great interest to study a series of cases of localized scleroderma to see if the sclerodermatous process can be retarded by administration of histamine by iontophoresis. Certainly over a fairly long period this can hardly injure the normal skin, and there would be a great advantage in continuously irrigating the connective tissues surrounding the sclerodermatous patches by means of the plasma of the patient himself. The acceleration of absorption and its attendant irrigation of the interstitial tissues by plasma may perhaps play a rôle in relieving the symptoms and retarding the development of the rheumatoid arthritic syndromes, as well as in those conditions for which galvanic therapy by means of histamine has been found so very useful.

COMPARATIVE STUDY OF CONVERSIVE HEAT AND IONTOPHORETIC MEASURES IN THE TREAT- MENT OF OSTEOARTHRITIS

SIDNEY LICHT, M.D.

Sixty-eight patients with osteoarthritis were treated in our Out-Patient Clinic with one of six different modalities of physical therapy. All were referred from the medical or orthopedic clinic with the diagnosis of arthritis. All had positive X-ray findings in the painful joint. No form of physical treatment had been used for three months prior to our observations. No concomitant treatment of any kind was permitted during our study.

A complete history was obtained. A physical examination was done on each of three visits, with the last examination being carried out one month following the date of the final treatment. The status at follow-up examination was recorded as the end result. At each examination, joints were measured whenever possible. All measurements were made by the same individual (the writer). The angle of motion range was determined with large calipers and a protractor; with the joint flexed, actively and passively, to the point of pain. The circumference of joints was measured with a flexible steel tape. While many patients knew when their joint had become larger or smaller, about ten per cent evaluated the change incorrectly, as determined by our own measurements. The subjective evaluation of angle range was more uniformly correct, but here, too, there were some errors, indicating the necessity for relying upon measuring instruments rather than the patient's memory in an accurate approach to a study on arthritis.

The modalities employed were: conventional and short wave diathermy, iontophoresis with mecholyl, histamine, sodium salicylate and plain water (positive galvanism). Each of these was given, in the routine manner of our clinic, for fifteen minutes, three times a week for seven consecutive weeks (20 treatments). All treatments were given at just below tolerance which, in administering histamine iontophoresis, was determined by permitting a generalized reaction at the time of the first treatment of each patient and then giving a dose of the same milliamperage, but of shorter duration, in subsequent visits.

The average age of all patients treated was 52.5. Only one patient was under 35. The duration of symptoms varied from three weeks to twelve years, with an average duration of thirty-one months.

The most frequent joint involved was the knee, either unilaterally or bilaterally, occurring in 39, or more than half the number of patients.

The next in frequency were the spine (11) and the shoulder (7). All other joints appear at least once in the series.

The results are listed according to three degrees of progress. 1. Relief, or complete disappearance of symptoms. 2. Improvement, to any degree whatsoever. 3. Failure; no change or worse.

In the entire group failure occurred in 40 per cent of the cases and relief in only 25 per cent. The remainder were improved. Of the total number treated, 71 per cent were female and 29 per cent were male. Although the number of failures was similar in each sex, being 40 per cent for males and 35 per cent for females, the number of those completely relieved was 45 per cent for males and only 17 per cent for females.

There was no selection of cases for treatment groups. The six modalities were employed in strict rotation as patients were admitted to observation. The unequal size of the groups was caused by the failure of some patients to complete treatment.

The following table shows the results obtained with each form of treatment, as well as a comparison of the combined heating groups and iontophoretic groups.

	RELIEF %	IMPROVEMENT %	FAILURE %
Short wave.....	34	32	34
Diathermy.....	27	45	28
Galvanism.....	28	30	42
Histamine.....	8	50	42
Mecholyl.....	18	55	27
Sod. salicylate.....	28	23	49
Conversive heat.....	30.5	38.5	31
Iontophoresis.....	18.5	41.5	40

If the criteria of evaluation of a good treatment depend upon the highest number of relieved and the lowest number of failures, then in our study of osteoarthritis, conversive heating was superior to the iontophoretic measures employed.

STATISTICAL EVALUATION OF TREATMENTS ADMINISTERED IN THE OUT-PATIENT PHYSICAL THERAPY DEPARTMENT OF THE MOUNT SINAI HOSPITAL DURING 1937

ALEXANDER HERSH M.D.

WITH THE COLLABORATION OF E. LEVY, M.D., S. LICHT, M.D., E. MARJEN, M.D.,
A. GUREVITCH, M.D., H. LEVANT, M.D., M. WEISS, M.D.

The purpose of this study is merely an attempt, by way of analysis and criticism of our procedures, to determine the clinical results obtained in patients referred to the Physical Therapy Clinic.

We fully realize that physical measures may not have been the only type of treatment which the patients received, and also appreciate that a more searching inquiry, which would concern itself with other types of treatment administered in other Departments, would be necessary for a more careful evaluation of the possibilities and limitations of the treatments available to the clinic type of patient who comes to this institution for relief.

From the so-called parent clinic the patient is referred to Physical Therapy for application of physical therapeutic measures. The major portion of the investigation of the patient's condition is done by other clinics. The referring physician sends us the patient when he believes physical therapy is indicated. Because of the great mass of material which presents itself to a large Out-Patient Department, it becomes necessary to treat as many patients as possible in the short space of time which is available. As a result of this there is all too frequently the tendency to dispose of cases by discharging or referring them to other clinics. Thus, in our Physical Therapy Clinic we treat as many as one hundred patients a day. What types of cases are referred to us? To what degree are we helping the patient?

In attempting to evaluate, we soon came to realize the limitation which confronted us. We recognized that the evaluation of the changes occurring should have been made by the physicians who referred the patients to us. Because of the difficulty in securing the patients' cooperation, this was not possible in most instances, and we therefore formulated our own opinion as to the outcome.

It is the practice in the Physical Therapy Clinic, for the physician who sees a new case to examine the patient and make his own diagnosis. If this concurs with the referring diagnosis the patient is accepted for treatment and physical therapy instituted. The treatment to be administered is outlined by the physician in Physical Therapy. If the diagnosis is not

the same as the referring one, the patient is sent back to the referring clinic with a request for reexamination and opinion. The matter is then discussed and a conclusion reached as to the working diagnosis.

In the process of collecting the data for this study, the individual physician in Physical Therapy who followed the patient made his own entry as to the type of treatment given, result, etc.

Until the new Physical Therapy Department of this hospital was opened, the types of treatment available were electro-therapy (consisting of convulsive forms of heat, and direct current and its variations), phototherapy, massage, exercise, ultraviolet and infra-red radiation, and paraffin casts.

Statistical evaluation of treatments administered in the out-patient physical therapy department of the Mount Sinai Hospital during 1937

	NUMBER OF CASES	IMPROVED	NOT IMPROVED
Involvement of structures about joints.	228	142 (62.2%)	86 (37.8%)
Low back pain	121	91 (75.2%)	30 (24.8%)
Pain (without diagnosis)	66	36 (54.5%)	30 (45.5%)
Bursitis	63	44 (69.8%)	19 (30.2%)
Fractures	52	51 (98%)	1 (2%)
Myalgias	24	24 (100%)	
Gynecological conditions	24	14 (58.3%)	10 (41.7%)
Bell's palsy	20	17 (85%)	3 (15%)
Trauma	16	15 (93.7%)	1 (6.3%)
Neuritis	16	8 (50%)	8 (50%)
Sprains	14	14 (100%)	
Neurosis	12	5 (41.6%)	7 (58.4%)
Local infections	11	10 (90.9%)	1 (9.1%)
Shoulder pain (without diagnosis)	9	8 (88.8%)	1 (11.2%)
Genito-urinary conditions	9	8 (88.8%)	1 (11.2%)
Paralysis	7	6 (85.7%)	1 (14.3%)
Sinusitis	7	4 (57.1%)	3 (42.9%)
Ear infections	6	6 (100%)	
Miscellaneous conditions	55		
Total	760		

There was no gymnasium and there were no hydrotherapy facilities. At a future date we hope to be able to compare the results obtained from the application of the modalities included in this study with the new ones which are now available.

This survey is confined to the period between January 1, 1937 and December 31, 1937. During this year 1,655 patients were treated. The actual number of treatments administered was 22,927; or approximately 2,000 a month. The review concerns itself with 760 of these patients who received treatments and attended the clinic until they were discharged; and their end results noted. The patients not included fall into three

groups: first, 573 patients who did not return for continued treatments and therefore no written notation as to the results of whatever treatment given is available. Second, 175 patients who received treatments during 1937, but who were discharged after December 31, 1937, and who therefore belong to the 1938 group. Third, 130 patients who received treatments during 1937 and are still being treated at the present time.

GROUPS OF DISEASES SURVEYED SEPARATELY

I. *Involvement of Structures about Joints—228 cases.*

A. Osteoarthritis—126 cases were referred to us under this diagnosis. There were 98 females and 28 males. The average age was 50.5 years. In 98 cases the diagnosis was made by the referring clinic and in 26 cases the diagnosis was established by the Physical Therapy Department. The duration of the condition before coming to the attention of our clinic varied from three days to sixteen years. The accompanying chart shows the modalities used and the results obtained.

B. Spondylitis—63 cases were referred to us under this diagnosis. There were 40 females and 23 males. The average age was 50.5 years. Sixty-two were white and one was colored. The duration prior to physical therapy treatment was one week to sixteen years. The diagnosis was made by the referring clinic in 43 cases and by the physical therapy clinic in 20 cases.

C. Periarthritis—17 cases.

D. Infectious arthritis—10 cases.

E. Stiff joints—9 cases. Four of these were postoperative joint cases.

F. Traumatic arthritis—2 cases.

G. Menopausal arthritis—1 case.

The results for the entire group of 228 cases were as follows:

Improved.....	142, or 62.2%
Not improved.....	86, or 37.8%

II. *Low Back Pain—121 cases.*

A. Low back pain (no etiological diagnosis)—68 cases. Of these 39 were females and 29 males. The average age was 50. Two patients were colored and sixty-six white. The duration prior to physical therapy treatment was five days to nine years. The diagnosis was made by the referring clinic in 63 cases, by physical therapy clinic in 5 cases.

B. Sciatic syndrome—27 cases.

C. Sacro-iliac disease—17 cases.

E. Sacralized 5 lumbar vertebra—1 case.

The results for the entire group of 121 cases were as follows:

Improved.....	91 cases, or 75.2%
No improvement.....	30 cases, or 24.8%

III. *Pain (without etiological diagnosis)—66 cases.*

These cases were referred as pain in various parts of the body.

Results of treatment for this group were:

Improved.....	36 cases, or 54.5%
Not improved.....	30 cases, or 45.5%

IV. *Bursitis—63 cases.*

A. Subacromial and subdeltoid bursitis—57 cases.

B. Olecranon bursitis—2 cases. Results of treatments with short wave:

Cured.....	1 case
Improved markedly.....	1 case

C. Prepatellar bursitis—4 cases. One case treated with short wave showed no improvement. Of three cases treated with diathermy, one showed slight improvement, one showed moderate improvement, and one showed marked improvement.

Results for the entire group:

Improved.....	44 cases, or 69.8%
Not improved.....	19 cases, or 30.2%

V. *Fractures—51 cases:*

Colles.....	20 cases
Lower leg.....	7 cases
Humerus.....	6 cases
Ankle.....	5 cases
Elbow.....	4 cases
Fingers and toes.....	5 cases
Patella.....	2 cases
Coccyx.....	1 case
Pelvis.....	1 case
Vertebra.....	1 case
Jaw.....	1 case
Hip.....	1 case

Results for the entire group:

Improved.....	50 cases, or 98%
Not improved.....	1 case, or 2%

VI. *Myalgias and Myositis—24 cases.*

Myalgia—10 cases.

Myositis—14 cases

Results for the entire group:

Improved.....	24 cases, or 100%
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VII. *Bell's Palsy—20 cases.*

Results:

Some degree of improvement.....	17 cases, or 85%
No improvement.....	3 cases, or 15%

VIII. *Trauma—16 cases.*

Results:

Some degree of improvement.....	15 cases, or 93.7%
No improvement.....	1 case, or 6.3%

IX. *Neuralgia and Neuritis—16 cases.*

Neuralgia—7 cases.

Neuritis—5 cases.

Meralgia paresthetica (symptoms referable to the distribution of the lateral external cutaneous nerve of the thigh)—4 cases.

Results for the entire group:

Improved.....	8 cases, or 50%
Not improved.....	8 cases, or 50%

X. *Gynecological Conditions—24 cases.*

Adnexal disease—17 cases.

Sterility—5 cases.

Postoperative adhesions—2 cases.

Results for the group:

Improved.....	14 cases, or 58.3%
Not improved.....	10 cases, or 41.7%

XI. *Sprains and Strains—14 cases.*

Strain—6 cases.

Sprain—8 cases.

Results for group:

Improved..... 14 cases, or 100%

XII. *Neurosis—12 cases.*

Results:

Improved..... 5 cases or 41.6%

Not improved..... 7 " or 58.4%

XIII. *Local Infections—11 cases.*

Results:

Improved..... 10 cases or 90.9%

Not improved..... 1 case or 9.1%

XIV. *Shoulder Pain—9 cases.*

Referred without any etiological diagnosis.

Results:

Improved..... 8 cases or 88.8%

Not improved..... 1 case or 11.2%

XV. *Genito-urinary Conditions—9 cases.*

Hypertrophy of Prostate—8 cases.

Epididymitis—1 case.

Results for group:

Improved..... 8 cases or 88.8%

Not improved..... 1 case or 11.2%

XVI. *Paralysis—7 cases.*

Hemiplegia—4 cases.

Ulnar nerve—2 cases.

Poliomyelitis—1 case.

Results for the group:

Improved..... 6 cases or 85.7%

Not improved..... 1 case or 14.3%

XVII. *Sinusitis—7 cases.*

Results:

Improved..... 4 cases or 57.1%

Not improved..... 3 " or 42.9%

XVIII. *Ear Infections—6 cases.*

Acute catarrhal otitis media—2 cases.

Acute purulent otitis media—2 cases.

External otitis—1 case.

Discharging mastoid sinus (postoperative)—1 case.

Results for the group:

Improved..... 6, or 100%

XIX. *Miscellaneous Group—55 cases.*

Paget's disease	2 cases
Epicondylitis	3 cases
Osteomyelitis	2 cases
Periostitis	3 cases
Rickets	1 case
Coccydynia	2 cases
Double weak feet	2 cases
Club foot	1 case
Slipped meniscus (knee)	1 case
Fibrositis	4 cases
Pruritis	1 case
Tenosynovitis	2 cases
Tumor	1 case
Thrombo-angitis obliterans	3 cases
Tuberculosis:	
Glands	3 cases
Wound	1 case
Nasal septum	1 case
Phlebitis	2 cases
Metatarsalgia	1 case
Electrosurgery	3 cases
Edema (etiology ?)	2 cases
Cardiac	2 cases
Anemia	1 case
Angioma	2 cases
Chest pain	1 case
Digital artery thrombosis	2 cases

COMMENT

The necessity for close cooperation between the Department of Physical Therapy and the other departments cannot be overemphasized. A firm adherence to the principle that the Physical Therapy Department be given as much prerogative as any other department in recording opinions, is essential. We have been most fortunate in that regard, and desire to express our thanks to all the other departments for their cooperation.

It is to be hoped that this and similar studies will more clearly indicate just what types of cases best respond to physical therapeutic measures; and will mitigate against the possibility of flooding the Physical Therapy Clinic with those conditions which do not respond to physical measures.

CONCLUSIONS

1. All of the myalgia and myositis cases showed improvement. All of the sprains and strains showed improvement.

2. More than 90 per cent of the fractures, trauma, and local infections showed improvement.

3. It appears that physical therapeutic measures are indicated in involvement of the structures about the joints, low back pain, bursitis, fractures,

myalgias, Bell's palsy, trauma, sprains, local infections, shoulder pain, certain genito-urinary conditions, paralysis, and ear infections.

4. Some form of physical therapy may be administered with some benefit in certain gynecological conditions; the same is true of sinusitis.

5. Sixty-six, or 8.6 per cent of the total number of cases were referred with the diagnosis "pain." Wherever possible the referring clinic should endeavor to give a more specific diagnosis.

Thanks are due to Misses Werthmann, Epstein, Tannenbaum, Cohen, and Lindeman, as well as to Mr. Bemis, for their assistance.

FEVER THERAPY IN GONOCOCCAL INFECTIONS

WILLIAM BIERMAN, M.D. AND CARL L. LEVENSON, M.D.

INTRODUCTION

Systematic attempts to treat gonococcal infections by temperature elevations were begun after Wagner-Jauregg's reports in 1918 (1). Various biological methods including malaria (2), typhoid (3, 4, 5) and other foreign proteins, such as milk, were advocated. Local heating of infected pelvic organs and joints by diathermy also received favorable comment (7, 8). The impetus toward the rapid progress in the treatment of gonococcal infections by physically induced temperature rises came from Whitney. In 1930 he accidentally discovered that temperatures could be raised in humans by exposure to the short waves of a radio transmitting apparatus (9). Since then many important simplifications and modifications have been introduced.

The successful search for a simple effective technique to treat gonococcal infections by induction of fever was due to one factor:—the thermolability of the gonococcus. The excellent results achieved by fever therapy were based upon the fact that this organism could be destroyed *in vitro* and *in vivo* at temperatures which human tissues could tolerate safely (6, 7, 10, 11). Although the factual basis for this work was begun by Neisser, it was really completed by Warren and Carpenter of Rochester University Medical School (8, 12). They were able to determine the thermal death times of more than 250 different strains of this organism and duplicated their laboratory findings in actual treatment of the human hosts.

TECHNIQUE

The method used at The Mount Sinai Hospital is based upon the principle that the higher the temperature, the less time is necessary for a gonococidal effect. While administering a systemic (rectal) temperature of 106°F. to 106.5°F., we differentially heat the pelvic tissues to a higher level, which in the female is between 109°F. and 110°F. The principle of this technique was first outlined in a memorandum from Dr. Bierman to Dr. Carpenter written in 1930. The effectiveness of this method was more easily demonstrable in the female because of the ease with which the pelvic organs and genito-urinary tract could be heated thoroughly by means of the vaginal electrode. Since the details of our methods have been described previously, only the general outlines are given here (11, 13, 14, 15).

The patient is carefully surveyed to rule out the presence of contra-

indications in the form of pulmonary disease or advanced changes in the cardiovascular system. The use of long maintained and effective local heating *in women* with relatively low elevation of the systemic temperature has permitted us to employ this thermolethal technique even in the presence of cardiovascular disease. The preparation consists of a cleansing enema and a light breakfast of tea and toast.

The systemic temperature is elevated by a horizontal light cabinet of special construction and short-wave current heating. When the desired rectal temperature is achieved, the auxiliary energy of the short-wave apparatus is discontinued and the four to six hours of pelvic heating in the female is begun. Only when a pelvic peritonitis is present do we defer the intensive pelvic heating for an additional three to four hours.

The technique of achieving this intensified pelvic heating has also been described (11, 13, 14, 15). Diathermy is the source and special electrodes (14) are used.

In the male, where necessary, pelvic and genito-urinary heatings are achieved by rectal diathermy or short-wave to the anterior urethra for two to three hours. The rectal mucosa is much more sensitive to heat than the lining of the vaginal vault and does not withstand long heating.

The systemic temperatures are maintained usually for ten to twelve hours. Sedation is achieved by fractionating doses of morphine and hyoscine hydrobromide. Close watch of the patient is always maintained. Temperature, pulse, respiration and color are watched continuously. During treatment, either iced tap water or cold 0.6 per cent saline by mouth is given freely. An intravenous of 5 or 10 per cent glucose in normal saline of 750 to 1000 c.c. is often administered after treatment.

It should be pointed out that all techniques in this field are secondary to the skill and judgment of the physician administering the treatment. Many kinds of apparatus are in use. The best of them become dangerous in careless or untrained hands. We insist on the continuous presence of a trained nurse and competent physician.

The necessity for retreatment is determined by positive spreads and the clinical picture. When warranted, the patient is retreated in the shortest possible intervals which, if possible, should be on alternate days.

CLINICAL DATA

The 165 cases of gonococcal infections presented in this report were treated through August, 1937, so that a sufficient follow-up period has intervened to permit accurate determination of results. Included in this series were 125 females, forty males, of which number forty were instances of gonorrheal arthritis. Every case included in this series had definite bacteriologic evidence of gonorrhea. About one-third of the females had salpingitis. Among the males, the usual complications of prostatitis (17

cases), involvement of vas deferens (5 cases) and epididymitis (8 cases) were present.

Of the 125 women, 117 (93 per cent) became bacteriologically free of gonococci and among the forty males there were six total failures—making a total of fourteen out of 165 upon whom fever therapy had no curative effect. The larger number of failures—five female and five males (10 of 14) received the shorter (6 hour) systemic bouts.

The average number of treatments among the *females* was 1.85 per patient. More than two-thirds of the fifty-five who were subjected to the longer ten to twelve hour sessions required only one treatment.

Within a few days of adequate treatment, there was a subsidence or disappearance of vaginal discharge. The cervical secretion became mucoid and clear. The cervical spreads contained only scattered leucocytes instead of previously found pus clumps. The urethral spreads became normal. In the salpingitis cases pain usually disappeared during the first treatment. These treatments may be given during any stage of the infection including acute salpingitis associated with fever and peritonitis. Tubo-ovarian inflammatory masses also responded satisfactorily. The pain diminished and then disappeared; temperature and sedimentation rates became normal.

Pelvic examination within a few days after treatment revealed marked diminution of pelvic tenderness. It usually took about a week before increased uterine mobility and shrinkage of masses became evident. During the ensuing weeks the adnexal masses gradually resolved. Patients noticed more normal and less painful menses after treatment. A number of our patients with acute salpingitis before treatment subsequently demonstrated normal tubal patency by the Rubin method. Some had normal pregnancies and deliveries subsequently.

The effect of fever therapy on the *males* was apparent during the course of each treatment. The purulent urethral discharge during the first half of the treatment became more profuse and then began to thin out and finally became watery. The typical intracellular organism first became extracellular, then larger, and finally changed staining characteristics before they would disappear. At the end of a successful treatment the spreads were completely negative and the thin, scanty, watery discharge contained a few pus cells and many epithelial cells without any trace of the gonococcus. Twenty-four hours after successful treatments the patient would be free of any signs or symptoms of the disease, although shreds in the urine persisted for varying periods.

Of the forty males, twenty-eight became free of the organism in from one to three treatments. The average was 2.8 per patient. Of the other twelve, six did not respond to subsequent treatment—apparently they were uninfluenced by fever therapy. These six failures were caused by

either insufficiently intense anterior urethral heating or inadequately sustained systemic elevations. Some refused more fever therapy and one was not permitted to undergo a second treatment because of his reaction to the first. Careful check-up and provocative tests were used to establish the permanence of the cures.

Gonorrheal Arthritis. The response of the systemic and joint manifestations of nearly all the arthritis cases was satisfactory and frequently dramatic. In all but eight of the forty cases joint symptoms subsided with remarkable uniformity immediately after the termination of treatment. Even in these eight there were changes for the better. Temperature elevations, malaise, chills and sweats, when present, disappeared. Sedimentation rates dropped toward normal and most of the patients were able to get out of bed within a short time after the successful treatments. The average number of treatments among the nineteen female and twenty-one male arthritics was 2.68 per patient: eight needed only one treatment. The largest number given any one patient was seven treatments.

Of the thirty-two cases among the arthritics, which responded to treatment, twenty-three needed no after-treatments to effect complete mobility of the involved joints. The other nine received diathermy or short-wave, radiant heat and light, and massage and corrective exercise to achieve normal motion.

The eight failures among the forty arthritics may be classified as follows: two came with permanent bony (x-ray) ankylosis; four had inadequate treatments, i.e. temperatures never over 105.5°F. and of too short duration; one, a female, had recurrence of pain and positive smears three weeks after discharge from the hospital, and reinfection by her consort was a possibility; one patient was infected by a heat resistant strain that would not yield to twelve hour treatments.

In gonorrheal arthritis, the duration of the disease before treatments apparently affected the response. Generally the longer the chronicity, the less rapid was the response. The danger of permanent damage to joint function also increased with duration. After-treatments to restore normal joint functions were more necessary in chronic than in acute cases.

It should be emphasized that the vast majority of these cases represented failures of other forms of treatment and that in this series, fever therapy accomplished what other therapeutic methods had failed to do. Furthermore, our results have been checked by time and the laboratory—some cases have been followed for five years.

Miscellaneous Complications. Among the miscellaneous gonococcal infections that have been reported as yielding to fever are the following: septicemia with purpura and arthritis (16); septicemia with endocarditis (17); and ophthalmia (18).

Sulphanilamide and Thermo-therapy. During the past year, a new and apparently important therapeutic weapon in the treatment of gonorrhea

has appeared—the drug, sulphanilamide. Although it is still too early to prognosticate the exact place this drug will have in the future treatment of gonococcal infections, nevertheless it unquestionably has been able to effect dramatic cures in an appreciable and perhaps large percentage of cases. The reports of the exact percentage of cures have varied widely. However, a definite number of failures have also been reported by every group describing the results with this drug. Since the use of sulphanilamide for gonorrhea has been advocated, we have urged that our patients, especially males, first submit to a possible cure by the simpler route of drug therapy. Our results with these patients in whom sulphanilamide failed have been to date about the same as with the previous series described in this paper.

Ballenger, Elder and McDonald (19) have reported that when they used sulphanilamide and thermotherapy (105°F.) for five hours, “simultaneously, they were more efficacious than when either was used alone.”

CONCLUSIONS

Physically induced elevations of temperature are effective in rapidly ridding the human host of the gonococcal invader. Because of the apparent success of sulphanilamide and its ease of administration, it is felt that, at present, only those patients, especially males, who have failed to respond to this drug therapy should be subjected to fever therapy. Fever therapy holds an important place in the treatment of gonococcal infections, especially among women; after failures with other methods and in the more complicated cases.

We wish to express our appreciation to Dr. E. A. Horowitz who contributed many important suggestions in the development of this treatment for the female, and who often actively assisted in the gynecologic care and treatment. We also desire to thank Dr. Robert Frank, Dr. George Baehr, and Dr. B. S. Oppenheimer for their cooperation and permission to use cases from their services.

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CLINICAL PATHOLOGICAL CONFERENCES

GEORGE BAEHR, M.D. AND PAUL KLEMPERER, M.D., *presiding*

Wednesday, November 10, 1937

Case 7. Accelerated Arteriosclerosis Terminating in Uremia (So-called Malignant Nephrosclerosis)

(From the Medical Service of Dr. George Baehr)

History (Adm. 413235). The patient was a 56 year old male who had had pneumonia five years prior to his admission to the hospital. He had been well until two years ago when occasional hematuria appeared; since then he had lost twenty-two pounds in weight and had had occasional attacks of dizziness and headache. One week before admission the patient was told that he had hypertension (above 200) and kidney disease.

Examination. The patient was well developed and well nourished. He was confused. His eyelids were edematous. There was marked proptosis. The fundi showed blurring of both discs and edematous venous compression. Scattered exudates and hemorrhages were also present. The chest was barrel shaped with crepitant râles at both bases. The heart was enlarged to the left. The blood pressure was 210 systolic and 160 diastolic. The liver edge was palpable three finger-breadths below the costal margin. There was slight dependent edema.

Laboratory Data. Hemoglobin was 62 per cent; red blood cells, 3,540,000; white blood cells, 13,400 per cu. mm.; the blood urea nitrogen, 67 mg.; creatinine, 6 mg.; phosphorus, 4.4 mg.; calcium, 10.3 mg.; cholesterol, 395 mg. per 100 c.c.

A flat abdominal roentgenogram revealed ring-shaped shadows in the renal vessels (calcification). An electrocardiogram showed regular sinus rhythm and left ventricular preponderance. The P wave was wide and notched. The PR interval was .20 to .21 seconds; the QRS was slurred; the RST was depressed in leads one and two; T1 and T2 were diphasic; T4 was inverted. The changes were interpreted as indicative of an enlarged left ventricle and myocardial abnormality.

Course. The patient ran a rapid down-hill course; despite intravenous therapy the blood urea nitrogen rose from 67 mg. to 99 mg. per 100 c.c. Death occurred eight days after admission.

Necropsy Findings. The kidneys were almost normal in size and of a striking dark bluish-red color. The surface was coarsely granular. There was no diminution in the width of the cortex. The vessels, on cross section, showed distinctly thickened walls and markedly narrowed lumina. Glomeruli could be seen as numerous pale dots in the cortex. The heart showed enormous hypertrophy of the left ventricle with a lesser degree of hypertrophy of the right ventricle.

Microscopically, there were marked and widespread lesions in the capillaries of the glomerular tufts and within the walls of the vasa afferentia. There were many foci of necrosis. The arteries of the kidney showed extreme narrowing of the

lumina due to marked thickening of the intima. Many fibroblasts were seen in this intimal thickening. This type of intimal change was seen in vessels of all sizes.

Comment. Dr. Klemperer referred to the lack of correlation between the gross anatomy and the clinical evidence of renal failure in this case. Microscopically, however, the cause for the uremia became apparent, in view of the widespread vascular lesions. He pointed out that the diagnosis of so-called malignant nephrosclerosis (the renal phase of accelerated visceral arteriosclerosis) can be made when there is an impairment of renal function associated with the anatomical findings in the kidneys of cellular thickening of the intima of small arteries and arteriolo-necrosis. The cellular intimal proliferation indicates a recent, i.e., an accelerated, arteriosclerotic change.

Dr. Baehr stressed the fact that 90 per cent of the instances of accelerated arterio-sclerosis occurred under the age of 50 years. Although this patient was older, his retinal vascular changes associated with only slight peripheral edema suggested the diagnosis clinically. Again a plea was made for abandoning the terms malignant sclerosis and malignant hypertension, for they only represent one of the final stages in which a case of primary hypertensive vascular disease may end.

Case 8. Chronic Diffuse Glomerular Nephritis with Retinal Vascular Lesions of the Terminal Accelerated Stage of Hypertensive Vascular Disease (So-called Malignant Sclerosis)

(From the Medical Service of Dr. B. S. Oppenheimer)

History (Adm. 407980). A 28 year old housewife, who had had scarlet fever at the age of 8 years, entered the hospital for the first time on July 7, 1936. Four years prior to her first admission a therapeutic abortion for pernicious vomiting, was performed when she was two months gravid at another hospital. She said that neither her blood pressure nor her urine were examined at that time. Three years later she developed an upper respiratory infection which persisted for two months. She then developed a chill with fever of 104°F., and severe pains in the ankles, wrists and small of the back. The urine was noted to be frankly bloody. The fever and hematuria persisted for two days, after which time acute tonsillitis became manifest. The latter subsided in one week. The following week there appeared a patchy erythematous lesion about the mouth consisting of red areas with dry scabs in the center, which gradually disappeared. She remained in bed for only two weeks after the onset of hematuria. Soon after she became ambulatory, nausea, vomiting, headaches and blurring of vision occurred. Three months before her first admission to the wards of the hospital she was examined in the Out-Patient Department of the hospital, where she was found to have kidney disease. When seen again, one week before admission, her blood urea nitrogen was found to be 60 mg. per 100 c.c. Her blood pressure was 210 systolic and 130 diastolic. It was because of these findings that she was hospitalized.

Examination. She appeared chronically ill and pale. She had puffy eyelids. Her fundi revealed pale discs with hazy margins, narrowed arteries and full veins; there were an occasional flame-shaped hemorrhage and scattered white exudates, while old exudates were seen in both macular regions. Moderate post-nasal discharge was present. The lungs were clear. The heart was enlarged to the left;

the A2 was greater than the P2 and booming in quality. The blood pressure was 230 systolic and 120 diastolic. Examination of the abdomen was negative.

Laboratory Data. The hemoglobin was 52 per cent; the white blood count, 10,700 per cu. mm., with 80 per cent polymorphonuclear neutrophiles. The urine showed two to three plus albumin and occasional granular hyaline casts. At times, two to three red blood cells were noticed per high power field. There was fixation of specific gravity at 1010 to 1012, as shown by the concentration test. The blood urea nitrogen was 63 mg.; creatinine, 5.5 mg.; chlorides, 375 per 100 c.c. Electrocardiogram revealed left ventricular preponderance and evidence of myocardial abnormality.

Course. It was recalled that the patient had had an uncomplicated attack of scarlet fever in childhood. In view of the fact that the blood pressure was found to be elevated at the time of the appearance of the hematuria six months prior to this admission, it was presumed that the patient had an exacerbation of an antecedent glomerulonephritis and therefore it was thought that she had a chronic glomerulonephritis with contracted kidneys. During her four weeks in the hospital the blood urea fell from 63 mg. on admission to 30 mg. at the time of discharge. Her blood pressure showed no significant change.

During the nine months between discharge and reentrance to the hospital she did poorly, lost about forty pounds in weight, and had recurrent transient attacks of nausea and vomiting, dyspnea on exertion and moderate ankle edema. In addition she had increasing episodes of nocturia (3 to 5 times). Two weeks before her second admission she developed pleuritis and a diffuse strawberry colored rash. This lesion gradually disappeared, leaving brown pigmented areas. One week before admission she suddenly began to pass bright red blood per rectum, which persisted to the time of her readmission on May 2, 1937.

Second Admission. The patient was dehydrated and appeared chronically ill. The fundi showed bilateral peri-papillary edema; the retinal arteries were irregular and thinned; soft white exudates radiated from the macula. The fundal picture was identical with that characteristic of the accelerated terminal stage of primary hypertensive vascular disease. The heart was slightly enlarged to the left by percussion. The heart sounds were of good quality; a soft systolic murmur was heard all over the precordium; the A2 was greater than the P2. The blood pressure was 180 systolic and 120 diastolic. Rectal examination showed the mucous membranes and perianal skin to be sodden, hemorrhagic and eroded. Several external hemorrhoids were present. The skin was the seat of numerous scratch marks.

Laboratory Data. The hemoglobin was 32 per cent; red blood count, 2,300,000 per cu. mm.; white blood count, 20,600, with 90 per cent polymorphonuclear neutrophiles. The blood urea was 185 mg. per 100 c.c.; the total protein was 6.6 (albumin 4.0, globulin 2.6). The urine showed a specific gravity of 1014, and was loaded with numerous white blood cells; neither casts nor red blood cells were seen.

Course. The night after admission the patient developed a generalized convulsion with twitchings of the arms and legs. No Chvostek or Trousseau signs were elicited. She received intravenous fluids and for the first three days the daily urinary output averaged 2000 c.c. Two days after admission she again suffered a generalized convulsion and following this developed a bilateral parotitis. The urinary output decreased markedly, she lapsed into coma and died eight days after her second admission.

Necropsy Findings. The kidneys were markedly contracted and together weighed 130 gm. The surfaces were diffusely and finely granular and pale yellow gray in color. On section, there was striking cortical atrophy and an increase in peripelvic fat. There were no noteworthy gross vascular changes. The heart weighed 360 gm. The walls of both ventricles were only moderately thickened. The lumina of the right circumflex coronary and its posterior descending branch showed thickening. There was acute myomalacia of the left posterior papillary muscle. A severe ulcerative colitis (uremic) involving the colon from the cecum to the sigmoid was present.

Microscopic examination of the kidneys revealed hypertrophy of the media of the small arteries and some slight intimal thickening, while occasional vessels showed almost complete obliteration of the lumina by a cellular proliferation of the intima. There was replacement fibrosis of the majority of the glomeruli and widespread tubular atrophy. There were, in addition, many areas of infiltration by polymorphonuclear leucocytes and lymphocytes.

Comment. Dr. Klemperer felt that in this instance one could, with comparative safety, make the diagnosis of chronic diffuse glomerulonephritis from gross examination of the kidneys, but cautioned that, generally, one should await the microscopic study for final diagnosis of a kidney lesion. He referred to the occurrence of vascular lesions in chronic diffuse glomerulonephritis and mentioned the appearance of arteriosclerotic vascular lesions which might be as severe as those observed in instances of accelerated nephrosclerosis.

Dr. Baehr stressed that the fundus changes were identical with those found in cases of accelerated arteriosclerosis, the terminal stage of primary hypertensive vascular disease. To make a diagnosis of chronic diffuse glomerulonephritis it was necessary to ignore the fundal picture of severe vascular disease, or to regard it as merely late secondary vascular alteration. The correct diagnosis in this instance was made on the basis of the history of scarlet fever in childhood and the story of frank hematuria occurring on the first day of an acute respiratory infection. The occurrence of hematuria on this first day of an acute respiratory tract infection is evidence of an antecedent glomerulonephritis. If the glomerulonephritis were acute, the hematuria would have occurred at least ten days or two weeks or more after recovery.

Case 9. Amyloid Contracted Kidneys

(From the Medical Service of Dr. George Baehr)

History (Adm. 410838). A 63 year old Russian male entered with a history of an occasionally blood-tinged, productive cough for twenty-one years. Chest X-ray examinations and sputum tests for tuberculosis were negative eight years previously. He suffered with dyspnea and occasional episodes of asthma for ten years. Three years prior to admission ankle edema and purpuric spots appeared which cleared with treatment. Four months ago edema, purpura and itching reappeared and had persisted. At that time he entered another hospital where hypoproteinemia, azotemia, moderate anemia, glycosuria, albuminuria, macroscopic hematuria and poor concentrating power were observed. Since that time anasarca, headaches, nausea, hypertension, twitchings and drowsiness had gradually developed.

Examination. On admission the patient appeared acutely and chronically ill, pale, dyspneic and orthopneic, with wheezing respirations and a productive cough. Flame-shaped hemorrhages were seen in both fundi; disc margins were blurred. The breath was urinous. The breath sounds were prolonged with râles at both bases. The heart was moderately enlarged to the left; sounds were of good quality. The blood pressure was 180 systolic and 100 diastolic. The liver edge was palpable two finger-breadths below the costal margin. Dependent edema was present up to the costal margins. There was twitching of the extremities.

Laboratory Data. The urine showed 3 plus albuminuria, with some red blood cells, some white blood cells and casts. Blood urea nitrogen was 120 mg.; creatinine, 17 mg.; sugar, 170 mg.; cholesterol, 470 mg. and phosphorus, 9.1 mg. per 100 c.c.; hemoglobin, 47 per cent; white blood count, 25,000 per cu. mm., with 92 per cent polymorphonuclear neutrophils.

Course. The patient was given a slow intravenous drip of blood with some apparent improvement in his condition. Twelve hours later his temperature rose

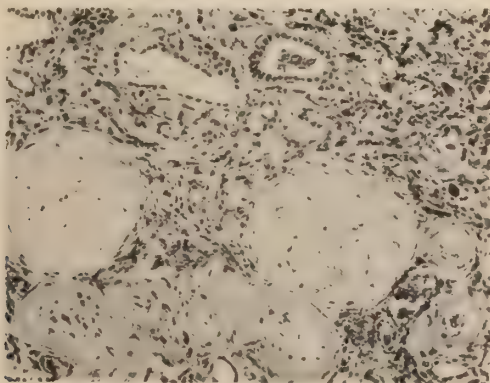


FIG. 1. (Case 9). Amyloid contracted kidney. Arterioles showing marked intimal proliferation with narrowing of lumina in addition to amyloid deposits.

to 100.8°F. and he developed pulmonary edema. Death occurred thirty-six hours after admission.

Necropsy Findings. The kidneys were contracted, weighing 145 grams together. They had a smooth finely granular pale yellow surface. There was marked narrowing of the kidney cortex. The heart showed only moderate hypertrophy of the left ventricle. The right ventricle, however, was markedly hypertrophied incidental to a chronic bronchitis and marked pulmonary fibrosis.

Microscopically, the kidney showed thickened fused glomerular tufts and an infiltration with a homogeneous eosinophilic substance (Fig. 1). This same infiltration was present within the walls of the smaller blood vessels. There was marked tubular atrophy and cellular infiltration of the stroma. The lumina of all the visceral vessels were strikingly narrowed, due to cellular proliferation of the intima. In addition there were occasional "foam cells" within the intima of some arteries—a finding usually present only in accelerated arteriosclerosis.

Comment. Dr. Klemperer said that the renal insufficiency was due to the severe renal amyloidosis with secondary contraction of the kidneys. An unusual finding

was the vascular changes similar to those encountered in instances of accelerated arteriosclerosis.

Dr. Baehr referred to the similar terminal clinical pictures presented by the three foregoing cases, each of which represented a totally different primary disease and etiology. All three cases, one of primary hypertensive disease, one of glomerulonephritis and one of amyloid disease, had developed advancing arteriolar nephrosclerosis. The advancing vascular disease and ischemic sclerosis of the kidneys had finally reduced the amount of surviving renal parenchyma to a point where renal insufficiency and azotemia resulted. The terminal clinical picture of dry uremia from progressive renal arteriosclerosis had finally replaced the more characteristic clinical picture of the primary disease. Dr. Baehr emphasized the fact that the retinal changes of all three cases were therefore basically the same. In spite of the fact that they are much more commonly observed in accelerated arteriosclerosis (malignant hypertension), the not infrequent occurrence of the hypertensive retinopathy with circumpapillary edema in other diseases of the kidneys obviates its differential diagnostic value to some extent.

Case 10. Hemocytoblastosis

(From the Pediatric Service of Dr. Bela Schick)

History (Adm. 408583). The patient was a 9½ year old white female admitted to The Mount Sinai Hospital on May 14, 1937. Six months before admission she developed a moderately severe sore throat and the same day a non-tender firm swelling was noted on the right side of the neck. Her temperature rose to 102°F. The sore throat and fever subsided after three days, but the mass in the neck gradually increased in size until the time of admission. Three weeks previously she began to have inconstant pain in both hips. During the past two weeks she had occasional pains in the lower abdomen and sternum. Temperature ranged from 99 to 101°F. She had lost four pounds in weight.

Examination. At the right side of the neck just behind the angle of the jaw there was a large, firm, fixed, non-tender mass measuring 8 by 5 cm. Additional small cervical and inguinal nodes were also palpable. The liver edge was felt 2½ cm. below the costal margin. The spleen was not felt. Situated in the midline and extending to a point about 4 cm. above the umbilicus was a large, hard, globular mass which seemed to extend from the symphysis. The mass was the size of an infant's head and freely movable. Rectal examination revealed a hard, globular mass in the left lower quadrant. The impressions of abdominal lymphosarcoma or ovarian malignancy with metastases were entertained.

Laboratory Data. Hemoglobin was 83 per cent; red blood cells, 5,000,000; white blood cells, 13,900; platelets, 370,000; polymorphonuclear neutrophils, 78 per cent; lymphocytes, 15 per cent; monocytes, 7 per cent. One lymphoblast was noted in the smear. The urine was negative. X-ray examinations of the long bones failed to show any abnormality.

Course. The temperature on admission was 100.5°F. Five days after admission a biopsy of the cervical lymph nodes was done and was reported as lymphosarcoma. Following this, radiotherapy was administered. The temperature showed daily variations from 101 to 103°F. Two weeks following admission the blood count revealed a large increase in immature cells. The white blood count had risen to

118,000 per cu. mm. The smear showed adult polymorphonuclear leucocytes, 33 per cent; young forms, 21 per cent; myelocytes, 5 per cent; eosinophiles, 6 per cent; lymphocytes, 6 per cent; monocytes, 3 per cent; myeloblasts, 2 per cent; chrom-myelocytes, 15 per cent; metamyelocytes, 9 per cent. In spite of irradiation, her condition became generally worse and dyspnea was more marked. The abdomen became increasingly distended, the cervical and abdominal masses more enlarged. She grew steadily weaker and died eighteen days after admission. A bone marrow puncture, performed three days after admission, revealed a slightly increased number of immature cells, but these were not considered sufficient to make a diagnosis of leukemia.

Necropsy Findings. The abdomen was markedly distended and contained 1300 c.c. of milky turbid fluid. The parietal pleura, pericardium and thoracic aspect of the diaphragm were studded with moderately hard nodular tissue. The liver and spleen were distinctly enlarged. There was generalized lymphadenopathy. The periaortic and pericaval lymph nodes were enormously enlarged and matted together into a firm mass (entirely) encasing the aorta and inferior vena cava. The right ovary was the size of a grapefruit and weighed 475 grams. The left was the size of a lemon and weighed 150 grams. The ovaries were irregularly nodular and on section displayed a homogeneous gray appearance with irregularly scattered red liquefied portions. The microscopic picture of the cells that had infiltrated all the organs showed them to be small, round and so immature as to be classed as hemocytoblasts. The post mortem bone marrow picture revealed 99 per cent myeloblasts of a very immature type.

Comment. Dr. Klemperer stated that the diagnosis of the biopsy tissue was lymphosarcoma, and pointed out that this was not an unusual error to make. An oxidase stain showed the presence of only relatively few positive cells because of the immaturity of the cells. Until shortly before exitus, the blood and bone marrow picture were normal. He emphasized that, due to proliferation of these immature cells, there was very little difference in the microscopic picture between an aleukemic hemoblastosis and that of lymphosarcoma. He stressed the fact that only when the peripheral leucocyte studies and the bone marrow showed enormous numbers of immature cells could one easily make the diagnosis of hemocytoblastosis.

Dr. Baehr suggested that since the blood and bone marrow changes appeared only shortly before death, and since the ovaries and lymph nodes were primarily involved, the origin of this hemocytoblastosis was essentially extramedullary, namely, in extramedullary foci of hematopoietic tissue. For this reason, abnormal cells were apt to escape into the blood stream before death and present a hematological blood picture resembling leukemia.

Reported by MARY C. TYSON, M.D.

Wednesday, November 24, 1937

Case 11. Hepar Lobatum—Syphilitic Cirrhosis of the Liver

(From the Medical Service of Dr. George Baehr)

History: (Adm. 403943). The patient was a 43 year old male. Twenty-five years previously he had had an attack of jaundice which lasted one week. He did

not recall whether he had any joint pains, fever or itching at that time. For many years he experienced post-prandial gaseous eructations and epigastric discomfort. Two months before his first admission he was told by his friends that he appeared pallid. He also noted that he was becoming more dyspneic and developed exertional palpitation. Four weeks ago his stools were noted to be tarry and three weeks ago he became aware of an increase in size of his abdomen associated with pruritis about the upper abdomen. Three days before admission he consulted a physician who advised hospitalization.

Examination. There was dullness at the right base; no râles. The heart was normal. The abdomen showed moderate distention in the flanks with numerous dilated veins. The edge of the liver and spleen were felt three finger-breadths below the costal margin. There were shifting dullness and a fluid wave. There was no icterus. The impression was cirrhosis of the liver with recent bleeding esophageal varices.

Laboratory Data. Hemoglobin was 38 per cent; red blood cells, 2,000,000 per cu. mm.; platelets, 120,000; white blood cells, 4,800; polymorphonuclear neutrophils, 81 per cent. The blood Wassermann reaction was four plus. The icteric index was 6; the Van den Bergh, 0.6 mg., indirect; total protein, 4.8 g. with 3.1 g. albumin and 1.7 g. globulin. The sodium benzoate test showed 3.92 g. excreted (normal). Cholesterol was 250 mg.; ester, 130 mg. Galactose tolerance test showed an excretion of 1 g. which was considered normal. Urine contained urobilinogen to a concentration of 1:20.

Course. The patient was treated with mercupurin in an effort to effect diuresis, and his anemia was treated with iron and blood transfusion. When it was learned that the patient had a four plus Wassermann, he was given 1 c.c. of Bismogenol every four days.

At this time the possibility of syphilitic cirrhosis of the liver was entertained, but Laennec's cirrhosis in a syphilitic was considered to be a more common association and was regarded as a better explanation of the clinical picture, especially of the ascites.

Under this regime his hemoglobin rose to 80 per cent and his ascites diminished. He lost ten pounds during his stay in the hospital. At the end of two weeks he was discharged to the care of his private physician.

Following his discharge from the hospital he remained well for about six months. Two months before his last admission, on August 22, 1937, however, his blood Wassermann was still positive in spite of continued bismuth therapy. He was able to work until two weeks before his final admission. At that time he developed an upper respiratory infection, with coryza, cold, and feverish feeling for about five days and a paroxysmal cough which was productive of some yellow mucoid sputum. On the afternoon before the second admission he suddenly vomited a small amount of dark red fluid. This recurred several times and was followed by transient syncope, during which he had an involuntary defecation. The stool was noted to be black. On the morning before admission he had two hematemeses the first one being about a cupful in quantity and the second one about a quart. His stools continued to be tarry.

Second Admission. The patient was a thin, pale, emaciated male. The sclerae were sub-icteric. Dullness and diminished breath sounds were heard over the

right lower lobe. The heart sounds were of good quality. The abdomen was slightly distended in the flanks. Slight shifting dullness was present. A coarse nodular liver was felt two finger-breadths below the costal margin. The spleen was firm and its edge was palpated two finger-breadths below the costal margin.

Laboratory Data. The hemoglobin was 36 per cent; red blood cells, 2,900,000; white blood cells 33,000, with 87 per cent polymorphonuclear neutrophils. The urine contained urobilinogen in dilution of 1 to 640. Cholesterol was 155 mg.; cholesterol ester, 18; total protein, 4.2 g.; albumin, 2.5 g.; globulin, 1.7 g.; icteric index, 2; bilirubin, 0.2 mg.; Takata-Ara reaction was negative. Blood Wassermann reaction was four plus.

Course. After admission it was learned that the patient had received some neoarsphenamine therapy from his private physician. The development of his icterus which progressed after admission was thought to be due possibly to arsphenamine toxicity in a person with Laennec's cirrhosis who happened to have a positive Wassermann.

He was given four transfusions. His course however was steadily down-hill. Bleeding was considered to be due to his esophageal varices on the basis of hepatic cirrhosis. The nodular character of the liver was commented upon and hepar lobatum secondary to syphilis was considered. Since such hepatic involvement is only rarely known to have caused portal obstruction, the diagnosis of Laennec's cirrhosis associated with latent syphilis was favored. The patient gradually lapsed into coma and died, ten days after admission.

Necropsy Findings. The liver showed the classical picture of hepar lobatum, with large deep cicatrizations. On section, one saw deep depressions into the liver tissue, due to connective tissue proliferation and associated regional atrophy. It was not the diffuse type of process characteristic of Laennec's cirrhosis; the normal lobular architecture was preserved in spite of the increase in fibrosis. Portal obstruction was attributed to this progressive replacement fibrosis. The spleen was large, weighed 650 g. and presented the fleshy appearance usually found in cirrhosis or portal thrombosis. The portal vein wall was thickened and moderately wrinkled in appearance. Such a process is observed with fair frequency in hepar lobatum, occasionally with thrombus formation. There was a recent thrombus in the splenic vein. Esophageal varicosities were found with two distinct foci of rupture. The aorta showed no evidence of syphilis. Histologic preparations of the portal vein revealed a diffuse cellular infiltration and thickening of the media and intima—a syphilitic phlebitis.

Comment. Dr. Klemperer and Dr. Baehr emphasized the fact that the clinical picture of Laennec's cirrhosis, including portal stasis sufficient to produce splenomegaly, ascites and bleeding from esophageal varices, may be the result of syphilitic cirrhosis of the liver. In spite of the fact that hepar lobatum is usually due to the intersection of the liver by the scars of numerous healed gummata, a diffuse hepatitis may be associated with the early stages of hepatic syphilis, which may subsequently give rise to a more diffuse cirrhosis. It was, therefore, a clinical error to eliminate the possibility of syphilitic liver disease in making the clinical diagnosis, in spite of the fact that the clinical picture was also characteristic of the more common Laennec's cirrhosis.

Case 12. Tuberculosis in the Puerperium

(From the Surgical Service of Dr. E. Beer)

History. (Adm. 407953). The patient was a 32 year old female who attended The Mount Sinai Hospital Out-Patient Department for "kidney disease" at the age of ten. The details of this illness could not be ascertained. For two years prior to admission to The Mount Sinai Hospital, she experienced occasional transitory pains in the right loin. These attacks at first occurred once every one to two months, but increased in frequency until they recurred once each week. About ten months prior to her admission the patient became pregnant. During the second month of her pregnancy she developed a dry, hacking, non-productive cough unaccompanied by any other symptoms. The cough persisted and became increasingly severe, particularly during the seventh month of her pregnancy. At about this time she noted a dull ache in the right loin and she began to have nocturia, which increased from one to five times since the onset. In addition, she developed increased diurnal urinary frequency, urgency and polyuria. Three weeks before admission she was seized with a shaking chill and developed a fever of 104°F. Her symptoms became steadily worse, fever continued for a week and she was admitted to another hospital where labor was induced. Immediately post partum there was slight abatement of loin pain but the chills and fever continued. The cough became productive of some white muco-purulent sputum and she began to suffer with severe night sweats. Four days after delivery her sputum was found to be positive for tuberculosis. She was admitted to this hospital fifteen days after the delivery of a normal infant.

Examination: The patient was an acutely ill, moderately dyspneic, pale female. The lungs showed only occasional medium, moist, scattered râles. The heart sounds were of poor quality; rhythm was tic-tac in character. The blood pressure was 120 systolic and 70 diastolic. The abdomen was moderately distended. There was slight costovertebral and loin tenderness on the right side. The uterus was enlarged to the size of a two months' gravidity.

Laboratory Data. Hemoglobin was 54 per cent; white blood cells, 14,000 per cu. mm.; polymorphonuclear neutrophils, 86 per cent; lymphocytes, 13 per cent; monocytes, 1 per cent. The urine was acid and contained 1 plus albumin, rare hyaline and finely granular casts and red blood cells. The blood Wassermann reaction was negative. Blood culture was sterile. Blood urea nitrogen was 11 mg. per 100 c.c.

Course. Temperature on admission was 99.8°F. but rose to 105°F. within eight hours. Two days later urography showed normal upper urinary tracts. The flat plate of the abdomen revealed marked enlargement of the liver and slight enlargement of the spleen. The patient continued to run a daily fever which reached 106.2°F. Gynecologic and urologic examinations were not revealing. Four days following her entrance a chest X-ray plate disclosed evidence of a moderate degree of infiltration of both lungs, which was most dense near the roots. It was impossible to differentiate roentgenologically between tuberculosis and metastatic neoplasm. Sputum examination done two days after admission showed innumerable acid-fast organisms. Fundal examination disclosed early choroidal tubercles, and tubercle bacilli were demonstrated in the urine. Following the establishment of these findings, the diagnosis of acute miliary tuberculosis was made.

A week after admission a friction rub was heard in the left lower anterior axillary region and occasional subcrepitant râles over both lower lobes. She went downhill steadily, developed slight nuchal rigidity and equivocal bilateral Kernigs, continued to have chills and fever and died with signs of an early tuberculous meningitis, two weeks after admission.

Necropsy Findings: The uterus was the size of a two months' gestation. The placental rest was high up on the posterior wall. There was no evidence of tuberculous involvement of the placenta, either grossly or microscopically. The lungs showed extensive tuberculosis of all lobes. The right upper lobe showed old chronic tuberculosis from which the exacerbation and spread had evidently originated. In this zone a calcified nodule was noted and adjacent to it a clover leaf lesion typical of recent bronchogenic dissemination. The other lobes showed extensive spread with numerous large and small clover leaf areas. In addition to yellow caseous areas, there were gray areas of gelatinous tuberculous pneumonia. Numerous small cavities had already been produced in many portions. Invasion of blood vessels was seen histologically with many intimal tubercles. The kidneys were the seat of numerous cortical yellow caseous nodules surrounded by red halos. The spleen was riddled with various sized tubercles. The intestine showed a large ulcerated mucosal lesion at the ileocecal valve.

Comment. Dr. Klemperer remarked that it was perhaps surprising that tubercle bacilli were present in the urine, in view of the fact that there was no involvement of the renal pelvis. He felt, however, that many large tubercles in the medulla could have been responsible for the appearance of tubercle bacilli in the urine.

Case 13. Hodgkin's Disease

(From the Medical Service of Dr. B. S. Oppenheimer and the Hematological Service of Dr. N. Rosenthal)

History: (Adm. 370789). The patient, a 39 year old unmarried woman, was well until four weeks before her first admission to the hospital in September, 1934. At that time she developed a dry, unproductive cough, fatigue, and noticed that she tired very readily on slight exertion. There were no chills, fever or chest pain. She also noted painless, non-tender swelling of the glands of her neck. Two weeks later she was seen by her physician who advised hospitalization and X-ray therapy.

Examination. The patient was a poorly nourished, chronically ill-appearing female with puffy face and somewhat cyanotic lips. The trachea was in the midline, partially fixed. A large group of firm, matted lymph nodes was found in the left supraclavicular fossa; a large node was present at the sterno-mastoid insertion and another below the right clavicle. There was moderate axillary and inguinal lymphadenopathy. There was a moderate increase in retromanubrial dullness. The lungs revealed dullness to flatness over the lower half of the right chest both anteriorly and posteriorly, and some dullness at the left base posteriorly. The breath sounds were diminished and also high pitched over the lower right chest. Fremitus was also impaired over these areas. There were no cardiac murmurs. The heart sounds were fair. The abdomen was very tense, the spleen being large and firm, occupying the left half of the abdomen and extending down to the level of the iliac crest. There was no evidence of ascites, and rectal examination revealed both fornices filled anteriorly and resistant; this was considered to

be due to lymph node enlargement. The blood pressure was 132 systolic and 86 diastolic, and equal in both arms. Laryngeal examination was negative.

Laboratory Data. Hemoglobin was 50 per cent; white blood cells, 32,800; polymorphonuclear leucocytes, 82 per cent; lymphocytes, 10 per cent; monocytes, 8 per cent. A chest X-ray examination revealed marked enlargement of the mediastinal lymph nodes on the right side and a large pleural effusion in the left chest. The diagnosis of Hodgkin's disease with mediastinal compression and invasion of the right lung was made.

Course. The patient ran a low grade fever up to 100°F. and, on one occasion, up to 101°F. Two days after admission a biopsy of an infraclavicular lymph node was done and was reported as showing Hodgkin's disease. The puffiness of the face and fullness of the neck veins with cyanosis of the upper extremities continued. Three days following her entrance, a thoracentesis yielded 20 c.c. of pale green fluid. The fluid disclosed a specific gravity of 1014 with 2500 cells per c.c.: all lymphocytes. The patient was given X-ray therapy with considerable recession of the effusion and diminution in size of the lymph nodes on the left side of the neck. The size of the spleen was unchanged. Twelve days later the patient was referred to the radiotherapy department for continuation of the treatment. One month after discharge the lymph nodes on the left side of the neck and the axillary and inguinal nodes had disappeared. The spleen had become strikingly smaller and now extended only to a point three finger-breadths below the left costal margin. During the next three years she continued to have X-ray therapy directed at the axilla and chest, depending upon the recurrence of lymphadenopathy. During her course of radiotherapy she became markedly anemic. This responded, however, to iron therapy and diet. In January 1937, she developed a nodule in the right breast and lymphadenopathy of the right side of the neck and behind the left mandible. The spleen became more easily palpable and was felt at a point five finger-breadths below the left costal margin. Subsequently infiltration of the left shoulder region involving the deltoid, and trapezius muscles developed. She gradually became weaker and lost weight. On July 3, 1937, she developed signs of bronchopneumonia over the left lower lobe. She was readmitted to the hospital with bronchopneumonia, right hydrothorax and edema of the back of the hands, and died two days after admission.

Necropsy Findings. The morbid anatomy was not typical of Hodgkin's disease because of the extensive fibrosis produced by the long period of X-ray therapy. The *spleen* was very large, firm and gray. It showed an unusual picture of extensive replacement fibrosis alternating with islands of splenic pulp. There were also scattered characteristic granulomatous infiltrations. A most unusual finding was an infiltration of the hilus of the pancreas. The *lymph nodes* and the splenic hilus showed typical involvement. The *liver* revealed no gross or microscopic changes. The *trachea* was surrounded by matted fibrous tissue and gray and anthracotic lymph nodes. There was also infiltration of granulomatous tissue into the surrounding areolar tissue and the right lung. The *right lung* was but one-half the usual size and showed evidence of widespread granulomatous involvement. There were zones of fibrosis, active cellular infiltrations and a widespread granulomatous pneumonia. Similar but less severe changes were found within the *left lung*. The bronchi were widely infiltrated and their mucosae ulcerated and thickened with here and there marked encroachment on the lumen.

Comment. Dr. Klemperer called attention to the extensive infiltration of the lung and felt that this was in favor of the view that Hodgkin's disease is inflammatory in nature. He said that the lungs are involved in 40 per cent of instances of generalized lymphogranulomatosis, but that an isolated pulmonary process without general lymphadenopathy is extremely rare. The parenchymal involvement in the case under discussion was believed to be due to extension from the pleura along the septae and then into the adjacent lung parenchyma with ultimate progression into the bronchi and blood vessels, i.e., invasion by contiguity. In some instances which came under his observation, the involvement had been so extreme as to completely occlude the bronchial lumen. Veins, too, have occasionally shown blockage of their lumen by the invading granulation tissue, and alveolar spaces, similarly, often undergo complete obliteration. Ultimately the granulomatous zones are replaced by firm connective tissue.

Dr. Baehr referred to the striking therapeutic result which was effected. He said that comparative statistics of treated and untreated cases have often misled the clinical observer concerning the value of X-ray therapy in Hodgkin's disease. They seemed to suggest that the average duration of the disease was influenced little, if at all, by X-ray therapy. The experience with this patient demonstrated the value of X-ray therapy on prolonging life. She would have succumbed three years before to mediastinal compression by enlarged lymph nodes if X-ray had not afforded prompt relief by inducing a rapid regression of the involved mediastinal nodes.

Reported by MARY C. TYSON, M.D.

Wednesday, December 1, 1937

Case 14. Multiple Hereditary Telangiectasia. Bleeding Duodenal Ulcer

(From the Medical Service of Dr. George Baehr)

History: (Adm. 408828). The patient, a 68 year old Russian male, entered the hospital on July 13, 1932 for the treatment of a nosebleed. The bleeding point was visualized just below the left inferior turbinate. The bleeding was controlled with cauterization and the patient was allowed to return home. He was readmitted three months later when he again suffered with a severe epistaxis which required cauterization. Three days before his third admission (March 13, 1934), he noted that his stools were black and tarry. These continued until entrance and were associated with increasing weakness and anorexia. At this time it was brought out that the patient had experienced frequent nosebleeds since childhood. Only one of his eight children was similarly affected. In addition, he had had a chronic cough with mucoid sputum for at least twenty years, the cough being worse at night. There was no story of gastro-intestinal symptoms.

Examination. Numerous telangiectases were scattered irregularly over the skin, buccal mucosa, lips, dorsal surfaces of the hands, under the fingernails, over the ears, nose, and forehead. Sibilant and sonorous râles were heard in the lungs and the chest was barrel-shaped. The heart sounds were of good quality. The blood pressure was 148 systolic and 82 diastolic. The clinical diagnosis was hereditary familial telangiectasia, the melena being ascribed to telangiectasia of the intestinal mucosa.

Laboratory Data. Hemoglobin was 58 per cent; red blood cells, 3,500,000; white blood cells, 8,400 per cubic millimeter with 60 per cent polymorphonuclear leucocytes. Bleeding and clotting times were normal. There were 280,000 platelets. The stool was black and gave a strongly positive guaiac reaction. The blood Wassermann reaction was negative. Rehfuess test meal showed a total acid of 90 units with free acid of 76, all specimens containing blood. A gastro-intestinal series showed a well filled duodenal bulb but a persistent incisura on the greater curvature of the duodenum. This was interpreted as indicative of a duodenal ulcer. Electrocardiogram revealed left axis deviation and a QRS of low amplitude, notched and slurred.

Course. The patient was placed on a soft diet. In addition he received reduced iron for his anemia and was given a course of mocassin venom injections (1 c.c. of a 1 to 3000 solution subcutaneously for twelve days). At discharge, seventeen days later, his stools were brown, sigmoidoscopy was negative, and he had no complaints. His hemoglobin, however, had risen only 2 per cent since admission. The diagnosis of duodenal ulcer was not definitely accepted by the clinicians at this time, and it was thought that the intestinal hemorrhage might have been the result of visceral telangiectasis. He left the hospital and at first gained about five pounds, although he continued to cough up about two ounces of white mucoid sputum daily. In addition, he had orthopnea and minimal dyspnea. The snake venom injections were continued in the Hematology Clinic. Three weeks before readmission, he began to have moderate sticking epigastric pain which occurred three or four hours after meals, and lasted only a few minutes. Eating relieved the pain. Two weeks before admission, he again noted tarry stools for three days. One week before entrance he had a small amount of lower extremity edema. Since his last discharge, occasional slight epistaxes had recurred.

Fourth Admission (September 25 to October 25, 1934). At this time, the findings were similar to those of the previous admission, except that the heart sounds were poor and there was a soft systolic apical murmur. The provisional diagnosis at this time included hereditary familial telangiectasia, chronic duodenal ulcer, generalized arteriosclerosis and coronary arteriosclerosis.

Laboratory Data. Hemoglobin was now 44 per cent with three million red cells per cu. mm. Rehfuess test meal showed a total acidity as high as 135 degrees with 120 degrees of free acid. The stools again gave a strongly positive guaiac reaction. Roentgen studies this time revealed an irregular duodenal bulb which was considered as definite evidence of a peptic ulcer.

Course. In spite of a Sippy diet and snake venom injections, the patient continued to have occult blood in the stools for three weeks. His hemoglobin, however, rose to 60 per cent and he was discharged, improved, at the end of a four week stay.

Fifth Admission (March 2 to 5, 1937). The patient remained well until December, 1936 when ankle edema reappeared. This finally extended up the lower extremities. Accordingly, he was digitalized but without improvement. He therefore returned to the hospital. At this time he was dyspneic, orthopneic and cyanotic. The lungs were clear; the heart sounds of poor quality, the rhythm totally irregular. The liver was felt four finger-breadths below the right costal margin. The other findings were similar to those already recorded.

Laboratory Data: Hemoglobin was 62 per cent, with 5,000,000 red blood cells per cu. mm. The venous pressure was nine cm. of water.

Course. The presence of right cardiac failure was evident. It was ascribed to pulmonary emphysema. On bed rest, digitalis, mercupurin and fluid limitation, signs of failure, particularly his edema, diminished considerably, and he was discharged to the clinic.

Sixth Admission (May 19 to 27, 1937). Edema was controlled by digitalis and mercupurin until one month before the final admission. He then developed repeated severe epistaxes, progressive weakness, and dyspnea with reappearance of edema of the legs. He appeared acutely ill and extremely dyspneic. The lungs were dull at both bases posteriorly with numerous crackling râles and diminished breath sounds. The heart and liver were as noted on the previous admission. There were marked cyanosis of the nail beds and clubbing of the fingers. Dependent edema was also marked.

Laboratory Data. Hemoglobin was 33 per cent, with 2,600,000 red blood cells per cu. mm. The stools again showed a strongly positive guaiac test.

Course. In spite of repeated small volume transfusions, digitalis and mercupurin, the patient lapsed into stupor and died eight days following his sixth admission. The clinical picture was attributed to right heart failure due to emphysema and the failure to respond to therapy was thought to be due to the profound anemia.

Necropsy Findings. The heart was markedly enlarged. The right atrium was enormously dilated and moderately thickened. The tricuspid valve showed thickening of its free margin and calcification of the ring. The right ventricle was markedly hypertrophied. The pulmonic ring was extremely dilated and the valve leaflets thickened and opaque. The main pulmonary trunk was tremendously widened and contained numerous intimal plaques. The mitral valve showed roughening and thickening of the free margin with thickening of the chordae tendineae as well. The papillary muscles were to some extent replaced by grayish fibrous tissue. The left ventricle showed only moderate thickening. The aortic valve leaflets were opaque with adhesions between two cusps. The lungs were markedly congested and edematous throughout, with some emphysema. The pulmonary artery ramifications were dilated and the smaller branches markedly thickened by flat yellowish plaques throughout. Microscopic examination showed severe thickening and narrowing of even the smallest arteries in some areas. The surface of the liver was covered with round umbilicated areas. On section, these nodules were seen to be yellow and showed an architecture similar to that of the normal liver. They varied from 0.5 to 2 cm. in diameter. The intervening tissue showed distinct deep red depressed central areas and yellow greasy periportal zones. The duodenum contained an ulcer on its posterior wall just beyond the pylorus. A large gaping sclerotic vessel could be seen in its base. The gastrointestinal tract contained a good deal of dark bloody fluid.

Comment. Dr. Klemperer stated that the absence of extensive pulmonary fibrosis suggested that the pulmonary arteriosclerosis may have been primary. Dr. Moschowitz felt that authentic instances of primary pulmonary arteriosclerosis were extremely rare and that the arterial lesions in this case could be explained on the basis of pulmonary hypertension consequent to emphysema. He further stated that the degree of hypertension in any case is not necessarily related to the

amount of emphysema, so that it would be impossible to say that the emphysema in this instance could not have been responsible for the increased pressure, and thus indirectly for the arterial lesions. Dr. Klemperer said, however, that the ordinary run of emphysema cases did not show such an extensive vascular lesion and that in this instance, therefore, another etiological factor might be responsible for the condition of the pulmonary arteries.

Dr. Baehr agreed with Dr. Moschowitz and stressed the point that a chronic cough had been present for more than twenty-five years. In his experience a chronic cough, even of extrapulmonary origin, may result in emphysema, and may be responsible for the development of hypertension in the pulmonary circulation and arteriosclerosis of the pulmonary arteries as in this case. That the emphysema was clinically significant was indicated by the presence of clubbed fingers.

Case 15. Toxic Cirrhosis of the Liver

(From the Medical Service of Dr. B. S. Oppenheimer)

History (Adm. 409121). The patient, a 42 year old female, was admitted to the hospital complaining of jaundice, nausea, vomiting and progressive enlargement of the abdomen. At the age of six, she had had an episode of icterus lasting six weeks. For many years she had drunk considerable quantities of whiskey. Six months before entering the hospital, she developed severe epistaxis which continued for many hours. This recurred frequently, sometimes as often as three or four times a week. In addition, she noted increasing weakness and pallor. A severe nose-bleed brought her to the Reception Ward six weeks before she was admitted. At that time, although she was icteric and had a large liver and spleen, she refused to enter the hospital. The jaundice gradually increased thereafter. Two weeks before admission she noted enlargement of her abdomen and experienced an episode of nausea and vomiting.

Examination. The patient was an emaciated icteric female with numerous small telangiectases of the face. The lungs were negative. A soft systolic murmur was heard at the apex. The abdomen was tense with ascites, and over its surface could be seen a wide venous network. The liver was firm and ballottable at the level of the umbilicus. The spleen percussed to a point one finger-breadth below the costal margin. Pitting edema was present over the sacrum.

Laboratory Data. Hemoglobin was 39 per cent; red blood cells, 2,200,000; white blood cells, 11,000; (80 per cent polymorphonuclear leucocytes) per cu. mm. Urine contained three plus bile; urobilinogen was present in dilutions from 1:10 to 1:40. Galactose tolerance test showed total excretion of 2.2 grams; sodium benzoate test 0.56. The lactic acid test showed impairment of liver function. The blood Wassermann reaction was negative. The icteric index was 35; the Van den Bergh, prompt positive; the total protein, 5.6 (albumin 2 g., globulin 3.6 g.). Takata-Ara reaction was four plus. Total cholesterol was 250 mg.; ester, 80 mg. per 100 c.c.

The clinical impression was Laennec's cirrhosis with a superimposed toxic hepatitis and hypoproteinemia.

Course. Two paracenteses were performed which yielded four and five liters respectively. The fluid was clear, but bile-stained, with a specific gravity of 1.008. One week after admission, the patient gradually lapsed into coma. The total

cholesterol dropped to 96 mg.; the ester to 37 mg. per 100 c.c. In spite of supportive therapy, the patient became gradually weaker passing into coma, and finally succumbed three weeks after entrance.

Necropsy Findings. The liver weighed 1900 grams. It was large and firm. The surface showed a coarse irregularity with numerous greenish yellow nodules varying from 5 mm. to 8 cm. in diameter, separated by depressed pink or red strands. The organ cut with increased resistance. The sectioned surface showed complete destruction of the normal architecture and was subdivided into large lobules of greenish yellow tissue. These, in turn, were incompletely subdivided into smaller lobules. The interlobular connective tissue was firm and grayish white with numerous vascular channels. The common bile duct was slightly thickened and had a dull, finely granular surface. The spleen was markedly enlarged (500 grams) and fairly firm. The surface was slate gray. On section, the Malpighian corpuscles could be seen only with difficulty. Microscopic study of the liver showed large nests of liver tissue separated by very vascular connective tissue strands which contained a few parenchymal cells. Some areas showed destruction of liver cells with only the stroma of the organ remaining. In these regions fibrosis was also present. There was an endophlebitis of the hepatic vein.

Comment. Dr. Klemperer described this as a case of old toxic cirrhosis upon which had been superimposed a recent episode of degeneration. Dr. Baehr said that the clinical diagnosis of Laennec's cirrhosis had been made because of the history of chronic alcoholism. He added that alcoholism might have been only one of the etiological factors since the patient had had an attack of jaundice in early life, forty-one years before the final episode. The first attack was, therefore, considered the primary phase of liver degeneration. He suggested the possibility that this early process, combined with the extensive use of alcohol, was responsible for the susceptibility of the organ to repeated attacks of hepatitis, which ended as a toxic cirrhosis.

Case 16. Retroperitoneal Myxoliposarcoma

(From the Medical Service of Dr. George Baehr and the Surgical Service of Dr. John Garlock)

History (Adm. 410578). The patient, a 60 year old woman, first entered the hospital complaining of dyspnea, a sensation of pressure in the upper abdomen and ankle edema. Five years before, she had begun to notice this heavy feeling in her abdomen and after two years was told by her physician that she had a cyst of the liver. The mass increased gradually until six months before admission when it began to grow more rapidly.

First Admission (June 4 to June 28, 1936). Two apparently discrete masses were felt in the abdomen. One was about the size of a large canteloupe, occupied the entire right side, and protruded forward. The other lay in the upper left portion of the abdomen. It was approximately the size of a large melon. Both masses were only slightly movable.

Laboratory Data. Hemoglobin was 58 per cent. Intravenous pyelogram showed mesial displacement of the right ureter. Barium enema revealed that the mass lay behind the colon and that the right colon was displaced to the left side of the abdomen.

Course. At operation, two days after admission, a huge retroperitoneal mass was discovered which had displaced the ascending colon to the left. It lay behind the colon and mesocolon but in front of the ureter. Its upper portion lay in front of the duodenum, head of the pancreas and stomach and extended practically to the diaphragm. The tumors were resected in three parts. The smallest was the size of a small coconut and the largest as big as a football. The pathological report by Dr. Klemperer was myxoliposarcoma. The patient had a smooth convalescence and was discharged at the end of three weeks.

Second Admission (June 24, 1937). For ten months the patient was rather well. She then began to have gaseous eructations, epigastric discomfort, and was moderately constipated. She gradually became weaker, her abdomen slowly increased in size, and there was a weight loss of six pounds.

Examination. The patient was pale and appeared chronically ill. The abdomen was soft, slightly distended, with shifting dullness in both flanks. A large rubbery non-tender mass, moving with respiration, extended across both upper quadrants as far down as the umbilicus. In the region of the gall bladder a tender tumor

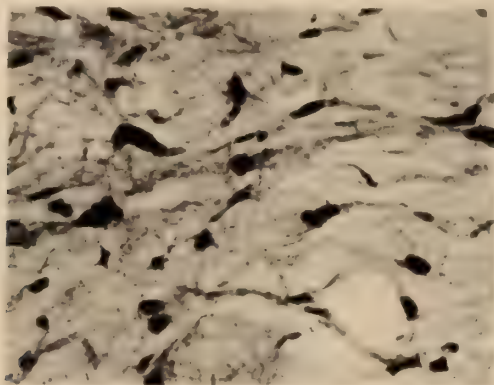


FIG. 2. (Case 16). Retroperitoneal myxoliposarcoma

about the size of a walnut was palpable. The impression at that time was that the patient had a recurrence of her tumor plus chronic cholecystitis and cholelithiasis.

Laboratory Data. Hemoglobin was 70 per cent; red blood cells, 4,300,000; white blood cells, 13,000 per cu. mm., with 76 per cent polymorphonuclear neutrophiles; the icteric index, 2.

Course. Laparotomy was performed eight days after admission. The lesser sac contained a football-sized mass. In addition, there were several smaller nodules lateral to the duodenum and numerous masses ranging from grape to melon size in the retroperitoneal space. Pathological examination revealed this tumor to be similar in nature to the original one. The patient died two days later.

Necropsy Findings. Immediately behind the hepatic flexure of the colon was a large irregularly nodular tumor measuring roughly 12 by 9 by 7 cm. Most of the mass was retroperitoneal, but it extended into the peritoneal cavity at the site of the foramen of Winslow where it almost completely encircled the bile duct. Posteriorly, it bulged into the anterior wall of the inferior vena cava without, however, invading it. Medially and anteriorly, the tumor had invaded the duodenum from

behind, and within the lumen of the bowel was an irregular mass 7 by 5 by 4 cm. Section of various portions of the neoplasm showed it to be lobulated and composed of rather firm, translucent, gelatinous gray tissue. Microscopic examination showed the typical picture of myxoliposarcoma (Fig. 2). The gall bladder was small and somewhat thickened. It contained a number of facettled cholesterol and pigment stones. The common duct was readily probed and bile was seen in the duodenum.

Comment. Dr. Klemperer stressed that although these tumors do not metastasize, they are prone to recur locally. Dr. Baehr pointed out that it was necessary, in the surgical treatment of such cases, to explore the retroperitoneal space carefully in order to discover and remove all the small nodules that might later result in recurrence. Dr. Arpad Gerster, former chief of the surgical service, thirty years ago, knew this type of tumor and repeatedly called the attention of his staff to the fact that retroperitoneal myxoliposarcoma is always arranged in multiple nodules. Usually the main mass is so conspicuous and so easily shelled out that the surgeon is tempted to close the abdomen without searching diligently for the minute nodules in the retroperitoneal space which give rise to recurrences.

Reported by ARTHUR SELIGMANN, JR., M.D.

CLINICAL NEUROPATHOLOGICAL CONFERENCE

JOSEPH H. GLOBUS, M.D., *presiding*

MONDAY, FEBRUARY 14, 1938

Case 6. Congenital Maldevelopment of the Brain. Dr. David Beres

History (Adm. 390219). The patient was a five year old Jewish girl who entered the hospital on February 24, 1936 with a history of recurrent convulsive seizures during a period of three years. Her birth was normal, but at the age of two weeks she developed stiffness of the left arm. It loosened up gradually, but in the course of the following month she had a series of similar attacks of stiffness lasting only a few seconds at a time, in which she became blue and cyanotic. When six weeks old, the patient began to have episodes of blueness and stiffness of the entire body lasting a few seconds. These attacks recurred until she was three months old. The further development of the patient appeared to be normal. The child sat up at six months, stood at ten months, walked at fourteen months and talked at the age of eighteen months. At this time she was noted to drag her left leg. When she was two years old she was struck on the head by a dropping toilet seat. There was no evidence of local violence to the skin, but ten minutes later, while being fed, she suddenly vomited, became unconscious and was seized by a severe generalized convulsion. She was taken to a hospital where the convulsions were stopped by an anesthetic. She remained unconscious for several hours. An X-ray examination of the skull revealed no fracture. Since then the child had many generalized convulsions and some lesser ones localized to the left arm. These attacks were preceded by either vomiting or epigastric distress. There were also occasions when the child would complain of a disagreeable sensation in the epigastrium without subsequent convulsions. In April, 1933 she had an exanthematous illness during which she had another convulsive seizure starting in the left arm and then becoming generalized. It was preceded by vomiting and was accompanied by unconsciousness and a rise of temperature to 108°F. Four months before admission to the hospital there was a particularly severe convulsion with the temperature rising to 105°F. Sanguineous cerebrospinal fluid was obtained. The child remained unconscious for several days, with the left lower extremity maintained in flexion. Then there followed a ten day period of semi-coma. At this time a change in speech was noted: the child spoke in a parrot-like fashion, unable to form complete sentences. Marked alteration in personality was also noted: she was easily frightened and became difficult to manage.

Examination. The little girl appeared well nourished. The face was fixed and bore the expression of a mental defective. She could not understand simple commands and did not react with any emotional display. The left palpebral fissure and the left pupil were larger than the right. The optic discs were normal. There was a left lower facial paresis and spastic paralysis of the left arm and leg. The deep reflexes were increased on the left side, with the abdominal reflexes being diminished on that side; there was a left Babinski sign.

Laboratory Data. The Wassermann tests of the blood and spinal fluid were negative. The cerebrospinal fluid was reported normal.

Course. On admission the diagnoses of a birth injury or a developmental defect affecting the right prefrontal area were considered. A vascular anomaly, a vascular tumor, or a porencephalic defect were also suggested as diagnostic possibilities. An encephalogram performed four days after admission revealed a marked internal hydrocephalus, the right ventricle being larger than the left. The third ventricle

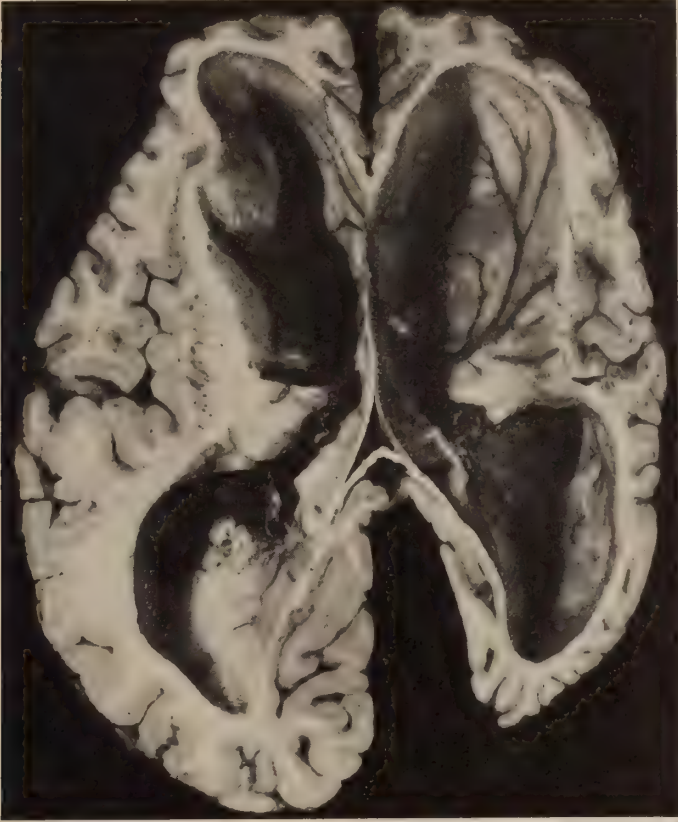


FIG. 11 (Case 6). Photograph of a section of the brain, illustrating the inequality of the two hemispheres and the marked internal hydrocephalus, as well as the abiotrophy (right) of brain substance.

was also distended. Two weeks later, on March 15, a ventriculography was done. No trace of indigo carmine was found in the ventricular fluid. It had been introduced into the spinal canal immediately before the ventriculography. The X-ray examination again showed marked internal hydrocephalus which appeared to be even greater than on the previous occasion. Following this procedure the child developed numerous convulsive seizures; and early papilledema appeared on the right side. A midline tumor was then considered as a diagnostic possibility. The papilledema became bilateral. On March 24, ptosis of the left lid and paresis

of the upward and outward movements of the left eye developed. On March 27, ventriculography with the use of thorotrast was done. It disclosed huge lateral ventricles, but the third ventricle was not visualized. On March 28, a suboccipital craniotomy was performed. When the cisterna magna was opened, the foramen of Magendie was visualized and found to measure more than one-half a centimeter in

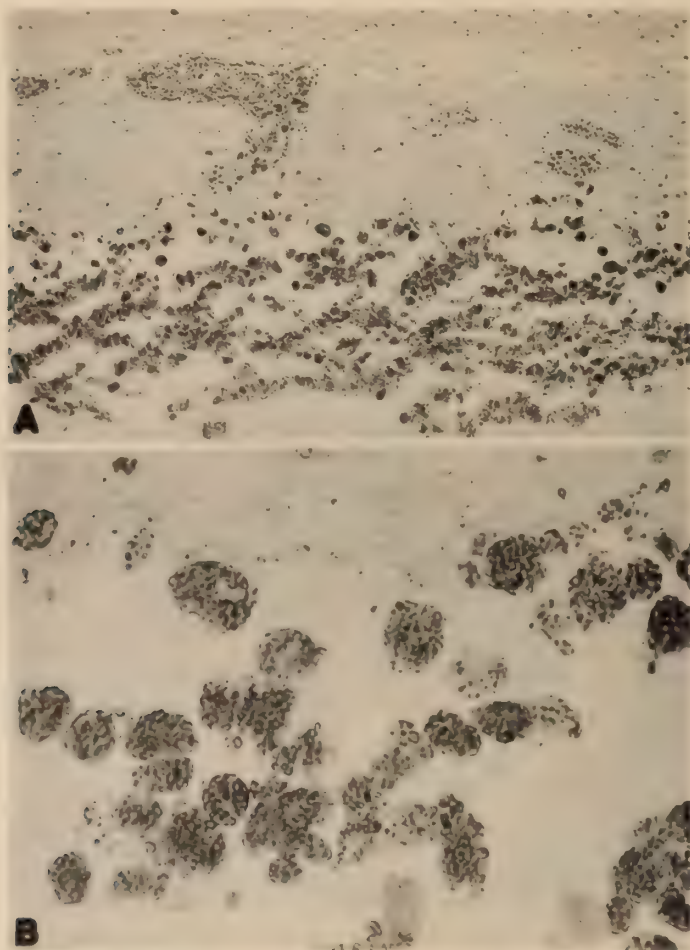


FIG. 12A (Case 6). The ependymal lining of the right lateral ventricle, its desquamation and the conversion of the ependymal cells into macrophages.

FIG. 12B (Case 6). Higher magnification of the ependymal cells shown in Figure 12A, displaying the granular appearance.

diameter. The fourth ventricle was enlarged. The surgical specimen removed at this operation consisted of a piece of pia arachnoid from the cisterna magna. It showed a chronic reactive leptomeningitis, secondary to a "subarachnoid hemorrhage." Following the operation the patient's condition became worse. On April 8, an abscess in the right thigh developed. This was incised and drained. The

spinal fluid, which had been clear on repeated examinations, became cloudy just before exitus. The temperature rose to 105.2°F. Violent convulsive seizures set in, and the child assumed a position of decerebrate rigidity. The patient died on April 23 during one of these spasms, eight weeks after admission.

Necropsy Findings. Gross Anatomy. There was a marked asymmetry of the two cerebral hemispheres, the right being smaller in all diameters (Fig. 11). On sectioning, two large lateral ventricles came into view, and, in spite of the small size of the



FIG. 13A (Case 6). The ependymal lining of the left lateral ventricle displaying only slight distortion and subependymal perivascular infiltration.

FIG. 13B (Case 6). The aqueduct of Sylvius, lined by intact ependyma, but containing macrophages free in its cavity.

right hemisphere, the right lateral ventricle was relatively larger than the left. The foramina of Monro were unusually wide open, and, similarly, the aqueduct and fourth ventricle were larger than normal. The ventral surface of the midbrain, pons, and medulla, showed an asymmetry, with the right side being reduced in volume.

Microscopic Anatomy. With lower magnification, it was apparent that the normal architecture of the cerebral cortex was lost. This was due to a marked reduction in the number of nerve cells and a relative increase in the glial elements, especially in the right hemisphere. The overlying meninges showed moderate thickening over the cortex but displayed a greater thickening at

the base, where the subarachnoid space was crowded with numerous macrophages containing coarse granules. The lining of the ventricles, particularly of the right lateral ventricle, showed marked alterations, such as desquamation of the ependymal lining (Fig. 12A) and the conversion of the ependymal cells into large macrophages containing granules (Fig. 12B). The alterations of the lining in the left lateral ventricle were less marked and were characterized by granulations and subependymal perivascular infiltration (Fig. 13A). The ependymal lining of the other ventricular divisions was relatively intact but was covered by macrophages (probably washed away from the right lateral ventricle (Fig. 13B)). Myelin stains revealed a reduction in size of the pyramidal tracts in the midbrain and hindbrain on the right side (Fig. 14).

Comment by Dr. Globus. In spite of the alleged normal birth, but in view of the onset of convulsive seizures as early as in the first two weeks of postnatal life, it is most probable that the defect in the brain was the result of some pathologic process



FIG. 14 (Case 6). Section of the pons showing atrophy of the right cortico-spinal tract.

which took place during the intrauterine life of the patient. The late stage of the defect and the character of the histologic changes in the parts involved indicated a developmental disturbance affecting the volume, distribution, and organization of the cellular elements of the cerebral cortex (5). The failure of the cortex, particularly that of the right hemisphere, to acquire its normal degree of development was paralleled by the failure of development of the related pyramidal tract.

What was still more significant was the fact that the alterations in the brain were progressive in character. With the passage of time, the patient manifested more and more evidence of an advancing brain distortion. This is readily understood when it is recalled that the developmental changes in the brain are not brought to an end at birth, but continue for a long period following birth. During this time cell migration and cell differentiation may assume a distorted character and give rise to changes which fall into the category of blastomatous alterations, as was probably the case in this instance.

Another observation of significance in this case was the deleterious effect of the

thorotrast upon the ependymal lining of the ventricle into which the substance was injected. There the ependymal lining desquamated and the loosened ependyma cells ingested the foreign substance. The substance, thus incorporated in the bodies of the cells, was no longer injurious to other parts of the lining of the ventricles, where these cells, crowded with the granules of the injected substance, were brought by the cerebrospinal fluid to rest upon intact ependyma. At the point of its maximum effect, the thorotrast, having stripped the ependyma, apparently broke through this defense line of the brain and entered the brain substance, as macrophages containing the thorotrast granules were seen enveloping blood vessels.

It is obvious from this case that thorotrast is not well tolerated by the brain and cannot be used with the belief that it offers no hazards to the patient.

Case 7. Thrombosis of the Right Posterior Inferior Cerebellar and Anterior Spinal Arteries. Dr. Eugene P. Mindlin

History (Adm. 399393). The patient, aged 46 years, was admitted to the hospital on October 7, 1936. He was known to have had hypertension since 1929. In the course of subsequent years he had several attacks of bleeding into the bowel, which were accompanied by tarry stools, jaundice, dizziness, and faintness. Following such attacks the patient would be confined to bed for three or four weeks and would then return to work. His fatal illness began in November, 1935, when he suddenly experienced a feeling of numbness in the right foot and soon afterwards felt a similar sensation in the right arm. In the course of that day there developed paralysis of the entire right side. His speech was not affected at the time. He took to bed and remained there for eight weeks. Improvement set in, with return of some power in the affected limbs, so that he was able to walk around a little, but could not, however, return to work. The physician who treated him reported that the patient's urine indicated the presence of kidney disease (nephritis). The patient's condition remained apparently unchanged until October 6, 1936 (twenty-four hours before admission to the hospital) when he suddenly became dizzy and began to vomit almost continuously. He swallowed fluids without difficulty but could not retain them. It was noted that his voice became markedly hoarse. He soon developed retention of urine so that he had to be catheterized. About 1000 c.c. of bloody urine were obtained. Shortly before admission the patient lapsed into a semi-comatose state.

Examination. The patient was in semi-coma; he could be aroused only with difficulty. His speech was slurred and thick. The pupils were unequal, the left larger than the right; both were slightly irregular, reacting sluggishly to light. Both eyes were deviated to the right. There was bilateral horizontal nystagmus on lateral fixation. A Horner's syndrome was present on the right side. The right corneal reflex was absent. There were a right central facial weakness, paresis of the right side of the palate and a right spastic hemiparesis, most marked in the lower extremity. The left extremities were also slightly spastic although they could be moved freely. All deep reflexes were slightly more active on the left side, with the exception of the ankle jerk which was more active on the right side. The abdominal reflexes were absent. There was a bilateral Babinski sign. Sensory examination revealed a diminution of sensation in all modalities, except for touch on the right side of the face and on the left side of the trunk and extremities. This examination was thought not reliable. Vibratory sense was apparently better on

the right than on the left side. This also was not fully reliable. The finger-to-nose test on the left showed no ataxia. This could not be tested on the affected side. The heart was enlarged to the left and there was a systolic murmur at the apex. There were dulness and râles over the right base. There was sclerosis of the peripheral arteries. The blood pressure was 210 systolic and 130 diastolic.

Laboratory Data. The blood contained 170 mg. of sugar per 100 c.c. The urea nitrogen was 30 mg. per 100 c.c. The white blood count was 14,500 per cu. mm., with 88 per cent polymorphonuclear neutrophils, 10 per cent lymphocytes and 2 per cent monocytes. The urine contained blood. The blood Wassermann test was negative.

Course. A diagnosis of closure of the right posterior inferior cerebellar artery plus multiple old vascular lesions on an arteriosclerotic-hypertensive basis was



FIG. 15 (Case 7). Section of the medulla oblongata at the level of its upper third showing the demyelinated areas. The latter are most pronounced on the right side and affect the pyramid, the median lemniscus, the spino-cerebellar tracts, and the descending tract of the trigeminal nerve.

made. The patient's condition was critical. He died on the day following admission.

Necropsy Findings. Gross Anatomy. The dura mater appeared normal. The leptomeninges were somewhat opaque, but showed no marked thickening. The gyri were somewhat flattened. The arteries at the base of the brain showed marked arteriosclerosis and numerous atheromatous plaques. The right vertebral artery was much thicker than the left. On opening the vertebral arteries the right vessel disclosed a thrombus formation and the left appeared almost occluded. On sectioning, a small area of encephalomalacia of old standing was found in the dorsal portion of the basis of the pons; no other areas of softening could be disclosed in the cerebral hemispheres.

Microscopic Anatomy. Sections through the medulla at the level of the middle of the inferior olive (Fig. 15) revealed areas of destruction, degeneration, and replace-

ment by deposits of fat. These changes affected the following structures: 1) the right and left pyramids, the latter only slightly; 2) the right medial lemniscus and the left medial lemniscus, the latter only moderately; 3) the right medial longitudinal fasciculus and the region of the right tectospinal tract; 4) the right ventral arcuate fibers; 5) the right dorsal spinocerebellar tract; 6) the spinal tract of the right trigeminal nerve; and 7) the right restiform body and part of the ipsilateral nucleus gracilis. At the level of the middle of the pons the affected areas were limited to the medial lemnisci, both of which showed large deposits of fat.

Sections of the cerebral cortex showed the leptomeninges to be thickened and to contain many red blood cells and lymphocytes. The intima of the blood vessels was fragmented in areas and the media was hyalinized, while the adventitia cells were swollen. The ganglion cells of the cortex presented various stages of degeneration with blurring and swelling of the nuclei. The glia of the subcortex was increased; there was also some satellitosis about the nerve cells.

Comment by Dr. Globus. This case well illustrates how a pathological process affecting a blood vessel may aid in the identification of the location and function of important structures in the brain. In this instance, a previous blocking of the posterior inferior cerebellar artery on the left side gave rise to a transient symptom-complex with some residuals; while the second time, as the result of the blocking of the right posterior inferior cerebellar artery, there developed a similar symptom-complex affecting the related parts with only this distinction—that the involvement of the anterior spinal artery had added a new feature to the symptom-complex. While the posterior inferior cerebellar artery supplies mainly the peripheral margin of the medulla, the anterior spinal artery supplies the ventral and central portion of this part of the stem. Thus, as a result of this double occlusion, the structures in both the central and peripheral portion of the medulla had become affected.

Case 8. Disseminated, Subacute, Productive Encephalitis of Unknown Etiology.
Dr. Edward Weinstein

History (Adm. 392864). A man, aged 38 years, apart from experiencing occasional vague epigastric pains, had been fairly well until three years before admission to the hospital (May 6, 1936), when he began to undergo a change in personality. More recently he became irritable, sullen, depressed, and easily angered, and on three occasions, without provocation, he beat his wife. This behavior was attributed to financial reverses. Three days before admission to the hospital he appeared to be dazed and seemed disinclined to speak. The following evening, on returning home following a search for a job, he suddenly began to cry, complained of headache and of epigastric pain, and vomited repeatedly and forcefully. Within a few hours his speech became unintelligible, but he appeared to understand what was being said to him. The next day he was noted to drag his right foot. His right arm was limp.

Examination. The patient appeared somewhat undernourished. He was unable to speak clearly, perseverating considerably. He could not carry out commands but was able to imitate a few gestures. The skull was tender to percussion, more so on the left side. The right palpebral fissure was slightly wider than the left. Both pupils were slightly irregular but reacted well. The nasal margin of the left disc was somewhat blurred. There was a right central facial weakness, a right hemiparesis with hyperactive deep reflexes, and a questionable Babinski

sign on the same side. The patient showed a mixed motor and sensory aphasia with marked apraxia and anomia.*

Laboratory Data. The cerebrospinal fluid was clear, contained 67 mg. of protein and 70 mg. of sugar per 100 c.c. The urine, blood, and cerebrospinal fluid tests were negative.

Course. A tumor in the left frontal lobe, encroaching upon the motor area, was diagnosed. The corpus callosum was thought to be involved. To ascertain this diagnosis an encephalography was performed, but no air entered the ventricles. Ventriculography was then performed and reported as giving evidence of a left-sided expanding tumor apparently situated anteriorly and parasagittally. This was based on the fact that there was a displacement of the interventricular

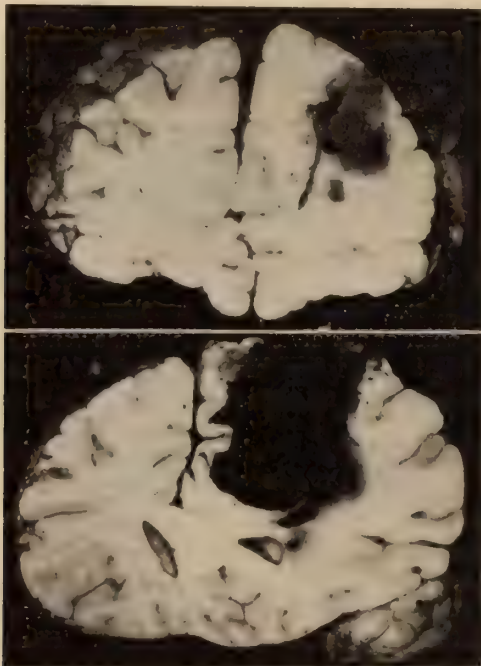


FIG. 16 (Case 8). A large hemorrhage in the left cerebral hemisphere

septum to the right, a depression of the left lateral ventricle, and conformity of the superior surface of the right lateral ventricle to a mass. There seemed to be a small amount of air in the third ventricle which was also displaced to the right. A craniotomy was then performed (June 1, 1936) and a cyst was encountered in the left frontal lobe. Tissue, which appeared to be degenerated tumor, was removed. The patient died the following day without regaining consciousness.

Necropsy Findings. Gross Anatomy. A large left parieto-temporal flap was present. When the brain was removed the left hemisphere was found to be larger than the right. All the gyri were flattened. In the left pre-Rolandic area there was an incision, the edges of which were macerated. In its depth there was considerable clotted blood, which was as large as a hen's egg.

On sectioning the brain, the left frontal lobe was considerably larger than the right and bulged beyond the border of the median longitudinal fissure, indenting the medial surface of the right frontal lobe, and involving the anterior portion of the corpus callosum. The tissue about the operative incision into the brain was soft. The operative incision opened into a large hemorrhage-filled cavity. In coronal sections (Fig. 16) the anterior extent of the lesion was found in the

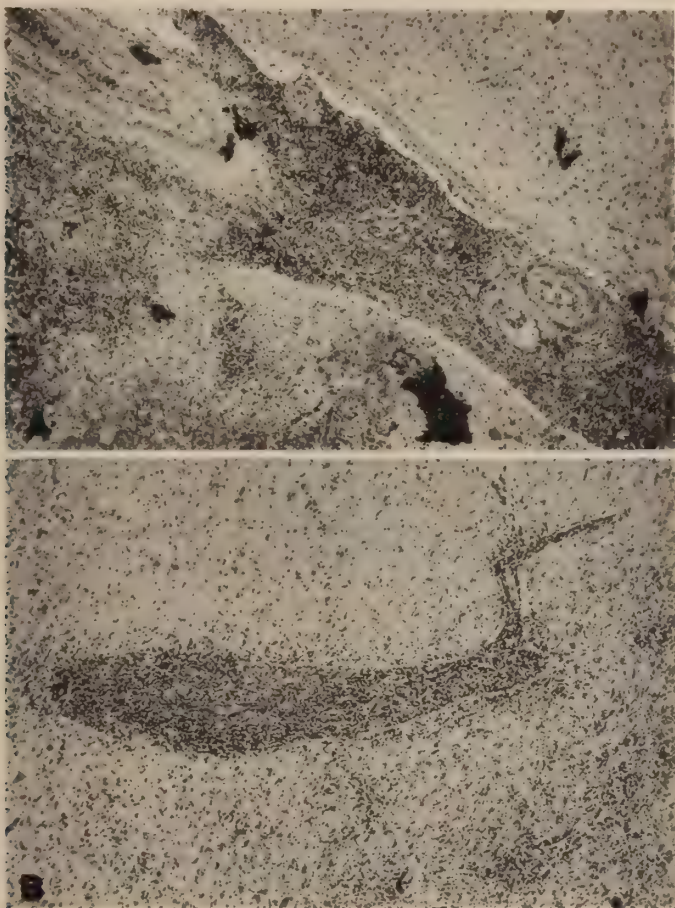


FIG. 17A (Case 8). The leptomeninges infiltrated by dense masses of mononuclear elements.

FIG. 17B (Case 8). Perivascular infiltration deep in the brain substance.

extreme left frontal pole; the posterior limit was just anterior to the anterior portion of the thalamus. In the region of the body of the lateral ventricle the cystic hemorrhagic lesion had eroded into the corpus callosum destroying practically its entire depth. The clot within the cavity was readily detached. There was marked distortion of the ventricle upward, corresponding to the apparent space-occupying lesion in the left frontal lobe.

Microscopic Anatomy. Widespread and irregularly disseminated inflammatory reactions were found throughout the cerebral hemispheres. They affected the meninges, cortex and subcortex. The meninges displayed dense infiltration with mononuclear elements (Fig. 17A) and this infiltration could be followed into the underlying cortex. Within the cortex, vessels with wide zones of adventitial infil-

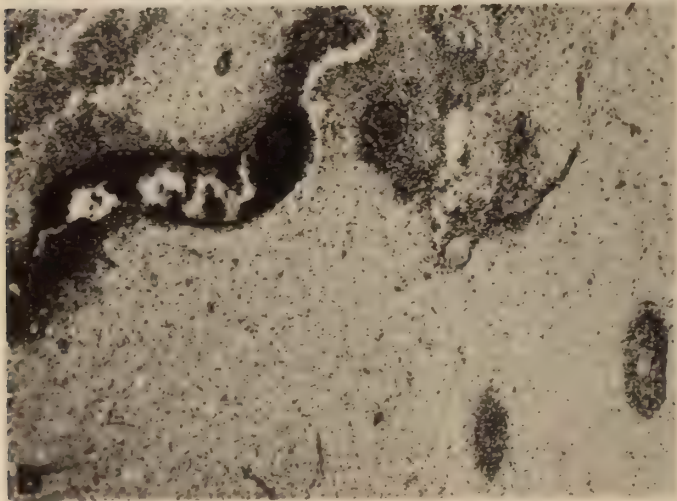
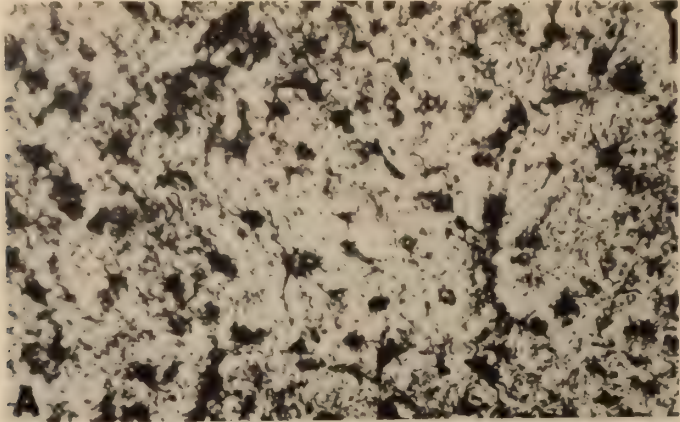


FIG. 18A (Case 8). Dense gliosis in the affected areas.

FIG. 18B (Case 8). Section revealing areas of disintegrating tissue in the neighborhood of infiltrated and necrosed vessels.

tration (Fig. 17B) were numerous. They, in turn, were surrounded by zones of glial infiltration (Fig. 18A) and more pronounced tissue disintegration (Fig. 18B). In other parts, thrombosed vessels were noted showing, in addition to disintegration of the vessel walls, areas of demyelination (Figs. 19A & B). Sections of the medulla oblongata revealed many corpora amylacea. Smaller vessels were encircled with small round cells, while larger vessels showed fairly advanced hyaliniza-

tion. These alterations indicated a subacute productive inflammatory process. The causative factor was obscure. No organisms could be demonstrated and a search for parasites was absolutely of no avail. There was still the probability that we were dealing here with a parasitic invasion, but search for *Torula* was unsuccessful.

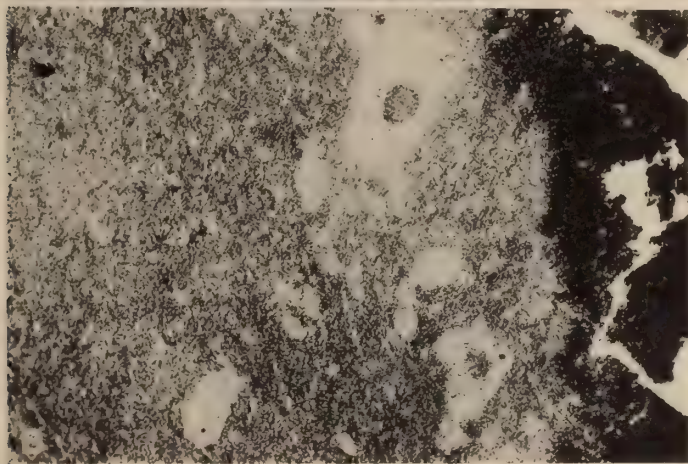
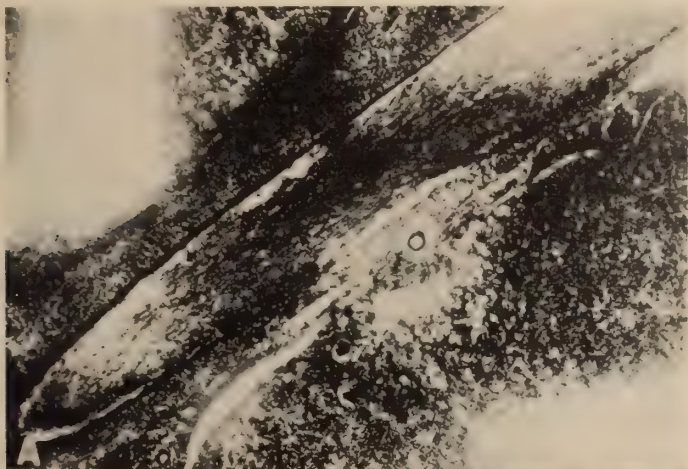


FIG. 19A (Case 8). A thrombosed vessel. Its wall and the surrounding tissue are undergoing disintegration.

FIG. 19B (Case 8). Areas of the brain showing demyelination about the affected blood vessels.

Comment by Dr. Globus. This case, in view of the inability to establish the etiological factor responsible for the productive inflammatory process, must remain an unsolved problem. The fact that in some parts the vessels showed marked thrombosis and disintegration suggested the diagnosis of necrotizing encephalitis. Even if such a diagnosis were accepted, it still would leave the problem unsolved,

for the term necrotizing encephalitis does not disclose the probable causative factor (6). The protracted course of three years' duration indicated the probability that we were dealing with a diffuse systemic disease in which the brain was just one of the several organs which had been involved. Unfortunately there was no full post mortem examination in this case. The presence of a hemorrhagic focus led one to suspect a parasitic invasion. The histological findings would be in accord with such a disease process, but again no parasites were disclosed in the tissue under examination.

Case 9. Amaurotic Family Idiocy. Dr. Jacob Friedman

History (Adm. 392053). A Jewish female child, fifteen months old, was brought to the hospital on April 16, 1936. There were two healthy older siblings, and, except for diabetes in a maternal grandparent, the family history was negative. The child appeared normal at birth, and had made seemingly satisfactory progress up to the age of six months. Thereafter she no longer would raise her head or make an attempt to sit up. She would not grasp proffered objects and would seem to fix her gaze on them for only a brief minute. Most of the time she would lie listlessly in bed. Occasional short spells of crying would cease when she was picked up. The child's hearing was described as acute. There were bursts of laughter of about twenty minutes' duration, which were described as "idiotic." During the week preceding her admission to the hospital she passed through episodes of transient muscular spasms affecting the extremities, associated with peculiar grimacing. Throughout this time she maintained good weight.

Examination. The patient was a well developed and a very well nourished infant of fifteen months. She lay quietly in bed, occasionally moving from side to side, but apparently indifferent to her surroundings. She exhibited marked hyperacusis, responding promptly to the slightest noise. She could raise herself to a sitting position but could not maintain it and her head would fall back. The tongue protruded through a wide open mouth and there was drooling of saliva. The anterior fontanelle was open and somewhat depressed. Excoriations were present over the buttocks and over the concha of the right ear. There were many palpable non-tender cervical lymph nodes. The pupils were round and equal, but did not react to light or in accommodation. The fundi revealed pallid nerve heads, particularly in their temporal halves. In each macula there was a central cherry red spot, surrounded by a grayish well-demarcated halo. This area was slightly elevated. The abdominal reflexes were not elicited. The extremities were flaccid and the deep tendon reflexes exaggerated.

Laboratory Data. The blood chemistry values were considered to be normal. The lecithin was 234 mg. per 100 c.c.; the total cholesterol, 190 mg. per 100 c.c.; the cholesterol with fatty acid cerebroside, 668 mg. per 100 c.c.; total fat, 1230 mg. per 100 c.c. of blood. The phosphatase content was 15 King-Armstrong units; the lipase, 0.37 c.c. n/20 sodium hydroxide required. A sternal marrow biopsy yielded 150,000 white blood cells per cu. mm.; there were 44 megakaryocytes per cu. mm.; the differential count was normal. A blood count showed: hemoglobin, 84 per cent; red blood cells, 4,550,000; white blood cells, 13,000; platelets, 400,000; polymorphonuclear neutrophils, 60 per cent; lymphocytes, 20 per cent; monocytes, 10 per cent with three containing vacuoles. The cerebrospinal fluid was clear and contained no cells. The urine was normal. The blood Wassermann

and the Schick, Mantoux and Pirquet tests were negative. Roentgenograms of the skull revealed a thinning of the bones of the calvarium and an unusually wide anterior fontanelle.

Course. The diagnosis of Tay-Sachs disease was made. Two weeks after admission the child developed a nasal discharge and a purulent discharge from the



FIG. 20A (Case 9). Note the marked swelling of the cell body, the spongy appearance of the cytoplasm of the nerve cells, the absence of tigroid substance and the peripheral displacement of the nucleus.

FIG. 20B (Case 9). A fat preparation of the cerebral cortex disclosing deposits of fat in the perivascular spaces and in the glial cells.

right ear. Food had to be administered by means of a gastric tube, since she no longer would swallow voluntarily. She declined rapidly and died on July 11, 1936 with signs of a bronchopneumonia.

Necropsy Findings. *Gross Anatomy.* The post mortem findings included bronchopneumonia, acute infectious splenic softening, fatty changes in the liver, and a patent foramen ovale. The anterior fontanelle was open, measuring one and a

half inches in the antero-posterior diameter. The posterior fontanelle was closed. The dura mater, leptomeninges and cerebral blood vessels appeared to be normal. The brain was uniformly increased in consistency. The left half, especially in the region of the occipital lobe, appeared to be larger than the right. The sulci were very marked and deep. The weight of the brain was 1125 gm. The spinal cord appeared to be normal.

Microscopic Anatomy. Widespread cellular alterations were noted in the entire cerebrospinal axis, affecting the cerebrum, cerebellum, brain stem, and spinal cord. They were characterized by the exceedingly marked swelling and spongy appearance of the cytoplasm of the nerve cells (Fig. 20A), the displacement of their nuclei to the periphery, and the almost complete loss of tigroid substance. The swelling had also affected the dendrites and axis cylinders, which displayed great irregularity in contour. Fat stains revealed practically no fat in the nerve cells but exhibited fat in the adventitial spaces (Fig. 20B) and in a relatively large number of glia cells.

Comment by Dr. Globus. The cell changes in amaurotic family idiocy are such as to indicate an inherent lack of potency for normal and sustained cellular development. The disease may be regarded as a form of abiotrophy. While ubiquitous in its distribution in the nervous system, it is nevertheless frequently restricted to the ectodermal components. Only occasionally do cellular structures undergo similar changes in other organs, and then the disease breaks through this limitation, affecting mesodermal as well as entodermal structures, as in the case of Niemann-Pick's disease. Since amaurotic family idiocy is a disease which begins very early in the developmental history of the individual and probably at the time before there were clinical manifestations, it is not improbable that it has its beginning at a very early stage in the differentiation of the nervous system. Under these circumstances the disease may be grouped with forms of malformation, the latter expressing itself in this disease in the alterations in the chemical and finer structural components of the cell (7).

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Edwin Beer

March 28, 1876–August 13, 1938

Edwin Beer was born in New York City on March 28th, 1876. His early education was obtained at the Columbia Grammar School and at Dr. J. Sachs' Collegiate Institute. He received his B.A. degree at Columbia College in 1896. In 1899 he received his medical degree from the College of Physicians and Surgeons, Columbia University. After his graduation he served his internship at The Mount Sinai Hospital in which institution he was an active member until the time of his death. After the completion of his hospital service, he engaged in post-graduate study in Prague, Berlin and Vienna. His first scientific papers, published in 1904, entitled "Adrenal Rests in the Liver," and "Diverticula of the Intestine," were early manifestations of that scientific urge which carried him to such heights. Very soon after his return from abroad he became associated with The Mount Sinai, Bellevue, Flower, and Lenox Hill Hospitals. In the latter hospital, he established one of the first departments of cystoscopy in the city. At about this time he became interested in neurological surgery and for a number of years was associated with Dr. Charles Elsberg at the Neurological Institute. When he was appointed attending surgeon to The Mount Sinai Hospital in 1910, he selected as his surgical specialty the field of urology which was then in its infancy. His numerous, original, brilliant, and fundamental contributions helped to place this specialty on the firm foundation which it enjoys today.

In an anniversary volume published by this Journal in March 1938, and dedicated to him, to mark the completion of thirty-eight years of active service at The Mount Sinai Hospital, Dr. Bransford Lewis summarized Edwin Beer's contributions to surgery and surgical literature as follows: "One is fairly amazed at their number, at their exalted merit and practical value, and finally at the great variety of subjects that he has studied, described, and oriented. While urology has furnished the basis for the greater part of his work, both operative and literary, he has gone afield for original contributions on other topics; gastro-intestinal pathology, diseases of the liver, the spleen, the spinal cord, and miscellaneous subjects. All of his writings have been serviceable in a practical way, and have on that account been studied by practitioners and students alike. They all show the logic of the philosophic mind that surveys his subjects in a broad conclusive way, relieved of the myopia that afflicts certain specialists of limited vision and restricted thought."

His crowning achievement in originality came in 1910, when he first

described a new treatment of bladder neoplasms employing the Oudin High Frequency Current. This new procedure helped to revolutionize the method of treatment of benign bladder tumors. For this great work, in 1927, he received the first Gold Medal ever awarded by the International Society of Urology at Brussels. He was again distinguished by the award of a Gold Key by the American Congress of Physical Therapy in 1937 for his pioneer work in the treatment of bladder tumors. His vast experience in the diagnosis and treatment of this disease furnished him with the exhaustive material embodied in a monograph on "Tumors of the Urinary Bladder," published in 1935.

Another outstanding achievement was his pioneer work in urologic diseases of children. He perfected the first practical infant's cystoscope which helped to simplify diagnostic urologic procedures in infancy and childhood. As a result of his extensive work in this field, urologic literature was enriched by the publication of a monograph on "Diseases of the Urinary Tract in Children" in 1930.

Edwin Beer served in France during the World War as a Lieut. Colonel in the U. S. A. Medical Corps. He was a member of numerous medical societies, both national and international in character. He served as President of The New York Surgical Society, Vice-President of the Academy of Medicine, and President of the Medical Board of The Mount Sinai Hospital.

Edwin Beer was liberal in giving—not only of his time, but also of his money, to all worthy philanthropic causes. He has passed from our midst but he leaves behind him the indelible memory of an individual who reached the pinnacle of his chosen profession through his scientific enthusiasm, his profound knowledge of his subject, his mature judgment, and his keen intellect. The medical profession lost in the person of Edwin Beer one of its most illustrious members and The Mount Sinai Hospital a distinguished surgeon. We who knew him intimately feel deeply the loss of a staunch friend, a teacher without equal, and a guiding spirit.

ABRAHAM HYMAN,

WILLIAM H. MENCHER.

Adolph Lewisohn

May 27, 1849—August 17, 1938

It is with deep sorrow that the Board of Trustees records the passing, on August 17th, of its beloved associate, Adolph Lewisohn, at the age of 89, after a life replete with good deeds, generous assistance to worthy causes, and personal coöperation in the carrying out of useful, constructive work for the benefit of his fellowmen. His philanthropies were wide and varied, extending to all activities in life and reaching all classes of persons in need of assistance.

In no field were his efforts more productive of lasting results than his work in behalf of The Mount Sinai Hospital. He was a member of its Board of Trustees from 1898 to the time of his death and he saw the hospital progress from the period when the new science of bacteriology was changing the nature of hospital service to the vast sphere of usefulness which it now fulfills in the general community. When Mr. Lewisohn first became a Trustee in 1898, the hospital was located on Lexington Avenue. At that time its Board had decided to erect a new modern hospital with vastly greater facilities than the original structure could furnish. The site chosen was the present one on Fifth Avenue. Competitive plans were called for and those of Mr. Arnold W. Brunner were selected. While the details of the new hospital were being considered, it was suggested that one of its principal features should be a Pathological Laboratory, the old hospital having only one room devoted to pathological research. This particular field of hospital work appealed strongly to Mr. Lewisohn, who volunteered to donate a building for the purpose. The offer was gratefully accepted and Mr. Lewisohn contributed the funds for the erection of the building, as well as for its equipment. He also provided a moderate amount to carry on its work, estimated at five thousand dollars a year, a substantial sum, though small in comparison with the full cost of maintaining the extended work of the present laboratory. In addition, Mr. Lewisohn agreed to donate five thousand dollars a year for five years to be paid towards the salaries of scientists employed in the laboratory. Dr. F. S. Mandelbaum was appointed head of the laboratory, Dr. Emanuel Libman acting with him in an advisory capacity.

The research work of the laboratory was most successful and the results fully equalled the expectations. The work of the laboratory grew to such an extent that it was deemed advisable to erect and equip a large new building in place of the old one to meet the additional requirements. Mr. Lewisohn again generously donated the cost of this new building, built in

1916, which now constitutes the present Pathological Laboratory of The Mount Sinai Hospital. The results of the research studies of this laboratory benefit not only the patients of The Mount Sinai Hospital but also the public generally.

Mr. Lewisohn was a member of the Laboratory Committee up to the time of his death. He repeatedly stated that, while deeply interested in the work of the hospital in general, he was particularly interested in its research work, which he felt had a more direct bearing upon reducing sickness, discovering new cures, making people healthier, prolonging life, and advancing medical science generally.

In the course of his life Mr. Lewisohn made large contributions to The Mount Sinai Hospital, and particularly to its Pathological Laboratory. His donations to the hospital aggregated over four hundred thousand dollars. He coöperated wholeheartedly with his fellow Trustees in enlarging the scope and value of the hospital and devoted much of his time and energy to bringing it to its present high standard of usefulness to the general community.

His passing, even at the ripe old age of 89, is deeply mourned by his fellow Trustees and the entire staff of the hospital. He will be remembered by his fellowmen for the many benefits which he bestowed upon them, not only by his work for Mount Sinai but by his liberal support and devoted coöperation in all good causes with which he was connected.

WALTER S. MACK, JR.

NEWS AND NOTES

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- MEDICINE CE 1—A course in diagnosis and therapy. Fee \$35. Drs. B. S. OPPENHEIMER, E. MOSCHCOWITZ, R. OTTENBERG, D. BECK and Staff of Second Medical Service. 3-5 p.m., Monday and Thursday. November 7, 1938-January 12, 1939.
- MEDICINE CE 3—Diseases of the kidneys and arteries. Fee \$15. Dr. E. MOSCHCOWITZ. 4-5 p.m., Thursday. December 22, 1938-February 9, 1939.
- MEDICINE CE 4—Diseases of the liver and biliary passages. Fee \$50. Drs. J. H. GARLOCK, P. KLEMPERER, S. S. LICHTMAN, R. OTTENBERG AND H. SOBOTKA. 1:30-3:30 p.m., Wednesdays, with three additional sessions on Fridays, 1:00-3:00 p.m., November 9, 1938-January 4, 1939.
- MEDICINE CE 5—General bedside therapy. Fee \$30. Dr. D. POLL. 3:30-4:30 p.m., Monday, Wednesday and Friday. November 7-December 30, 1938.
- MEDICINE CE 6—Clinical manifestations of coronary artery disease. Fee \$25. Drs. E. P. BOAS and H. LEVY. 3-5 p.m., Monday. November 7-December 26, 1938.
- MEDICINE CE 8—Practical hematology. Fee \$35. Dr. N. ROSENTHAL. 2-4 p.m., Monday and Thursday. November 7-December 29, 1938.
- MEDICINE CE 9—Clinical electrocardiography. Fee \$35. Drs. A. M. MASTER, H. L. JAFFE AND S. DACK. 1:00-3:00 p.m., Friday. November 11, 1938-January 13, 1939.
- MEDICINE CE 13—Allergy in relation to internal medicine. Fee \$50. (for combined course). Drs. J. HARKAVY, H. A. ABRAMSON AND A. ROMANOFF. 9:30-11:30 a.m., Monday, Wednesday and Friday (\$35, if taken alone) 2:30-3:30 p.m., Monday, Wednesday and Friday (\$25, if taken alone) November 7-December 30, 1938.
- MEDICINE CE 15—Practical course in peripheral vascular disorders. Fee \$25. Dr. S. SILBERT. 9:30-11:00 a.m., Thursday. November 10, 1938-January 26, 1939.
- MEDICINE CE 16—Clinical cardiology with particular reference to endocarditis. Fee \$35. Dr. S. H. AVERBUCK.
- MEDICINE CE 19—Clinical bacteriology and immunology. Fee \$30. Dr. G. SHWARTZMAN. Hours to be arranged. November 7-December 30, 1938.
- MEDICINE CE 20—Practical course in clinical bacteriology. Fee \$25. Miss C. HERSCHBERGER. Hours to be arranged. November 7-December 30, 1938.

DISEASES OF CHILDREN

- DISEASES OF CHILDREN CE 1—Clinical pediatrics: A comprehensive course in diseases of children. Fee \$35. Drs. B. SCHICK, H. SCHWARZ, M. H. BASS,

- B. S. DENZER, J. L. KOHN, S. KARELITZ, A. E. FISCHER AND G. J. GINANDES.
3-5 p.m., Tuesday and Thursday. November 8, 1938-January 3, 1939.
- DISEASES OF CHILDREN CE 2—Nutrition of infants and older children. Fee \$25.
Dr. B. SCHICK. 3-4 p.m., Tuesday and Thursday. November 8-December 29, 1938.
- DISEASES OF CHILDREN CE 3—Heart disease in children. Fee \$35. Dr. I. R. ROTH. 9:30 a.m.-12:00 n., Saturday. November 12-December 31, 1938.
- DISEASES OF CHILDREN CE 4—Conduct disorders of children. Fee \$25. Dr. I. S. WILE. 2-4 p.m., Wednesday. November 9-December 28, 1938.
- DISEASES OF CHILDREN CE 5—Asthma in children. Fee \$25. Dr. M. M. PESHKIN. 3:30-5:30 p.m., Friday. November 11-December 30, 1938.
- DISEASES OF CHILDREN CE 6—Diabetes mellitus in children. Fee \$35. Dr. A. E. FISCHER. 9:00-10:30 a.m., Saturday. Other hours to be arranged. November 12-December 31, 1938.

OPHTHALMOLOGY

- OPHTHALMOLOGY CE 1—Ophthalmoscopy. Fee \$50. Dr. K. SCHLIVEK. 3-4 p.m., Monday and Thursday. November 7-December 15, 1938.
- OPHTHALMOLOGY CE 2—Slit lamp microscopy of the living eye. Fee \$35. Dr. R. K. LAMBERT. 3-4 p.m., Thursday. November 10-December 29, 1938 or January 5, 1939.
- OPHTHALMOLOGY CE 3—Ophthalmic surgery. Fee \$75. Dr. H. MINSKY. 4-6 p.m., Monday and Thursday.
- OPHTHALMOLOGY CE 4—Refraction and Muscles. Fee \$50. (if taken combined). Refraction, alone, \$35; Muscles, alone, \$20. 2-4 p.m., Monday; 4-5 p.m., Wednesday. November 7-December 28, 1938.
- OPHTHALMOLOGY CE 5—Histo-pathology of the eye. Fee \$60. Drs. J. LAVAL AND D. WEXLER. 8-10 p.m., Friday. October 7-November 25, 1938.
- OPHTHALMOLOGY CE 6—External diseases of the eye. Fee \$35. Dr. D. WEXLER. 2-4 p.m., Friday. November 8-December 27, 1938.
- OPHTHALMOLOGY CE 7—Embryology of the eye. Fee \$35. Dr. A. L. KORNZWEIG. 3-5 p.m., Wednesday. November 9-December 28, 1938.
- OPHTHALMOLOGY CE 8—Ophthalmic neurology. Fee \$35. Dr. M. A. LAST. 4-6 p.m., Tuesday. November 8-December 27, 1938.

GYNECOLOGY

- GYNECOLOGY CE 1—Dr. Rubin's Service: Clinical course in gynecology together with a survey of gynecological pathology. Fee \$60. Drs. I. C. RUBIN, M. A. GOLDBERGER, P. BERNSTEIN, S. WIMPFHEIMER AND E. KLEMPNER. 9:30-10:15 a.m., Monday, Wednesday and Friday and other hours. November 7-December 31, 1938.
- GYNECOLOGY CE 1—Dr. Geist's Service: Gynecological diagnosis, treatment and pathology. Fee \$60. Drs. S. H. GEIST, M. D. MAYER, U. J. SALMON, J. A. GAINES AND M. E. MINTZ. 8:45-9:30 a.m., Monday, Tuesday, Wednesday, Thursday and Friday and other hours. November 7-December 31, 1938.

PHYSICAL THERAPY

- PHYSICAL THERAPY CE 1—Physical therapy for the general practitioner. Fee \$50. Drs. W. BIERMAN, C. L. LEVENSON AND S. LICHT. 9:30-11:00 a.m., Tuesday and Thursday. November 8-December 29, 1938.

LABORATORY METHODS

CHEMISTRY CE 1—Pathological chemistry. Fee \$30. Dr. H. SOBOTKA. Hours to be arranged. November 7–December 30, 1938.

CHEMISTRY CE 2—Routine chemical methods as used at The Mount Sinai Hospital. Fee \$35. Miss M. REINER. Hours to be arranged. November 7–December 30, 1938.

GASTROENTEROLOGY

MEDICINE CE 31—Diagnosis and treatment of diseases affecting the gastro-intestinal tract. Fee \$50. Drs. B. B. CROHN, A. WINKELSTEIN, E. GRANET AND H. YARNIS. 9:30–11:30 a.m., Monday, Wednesday and Friday; 3–5 p.m., Thursday. November 7–December 30, 1938.

PROCTOLOGY

PROCTOLOGY CE 1—Intensive course in office proctology. Fee \$50. Drs. S. D. MANHEIM, J. H. GARLOCK, A. GOLDSCHMIDT, L. J. DRUCKERMAN AND H. PESKIN. 9:30–11:30 a.m., Wednesday and Friday. November 9–December 30, 1938.

PSYCHIATRY

PSYCHIATRY CE 1—Psychoanalysis in medicine. Fee \$25. Drs. C. P. OBERNDORF AND A. SLUTSKY. Hours to be arranged. November 8–December 30, 1938.

PSYCHIATRY CE 2—Clinical work in mental diseases. Fee \$25. Drs. C. P. OBERNDORF AND S. LORAND. Hours to be arranged. November 8–December 30, 1938.

ORTHOPEDICS

ORTHOPEDICS CE 1—Clinical orthopedics. Fee \$25. Drs. R. K. LIPPMANN, S. SELIG, E. M. BICK AND A. J. SCHEIN. 3–4 p.m., Monday and Thursday. November 7–December 29, 1938.

Second Series

GENERAL MEDICINE

MEDICINE CE 2—Diseases of metabolism and practical dietetics. Fee \$35. Drs. G. BAEHR, H. LANDE, H. POLLACK, L. SOFFER AND D. ADLERSBERG, Miss A. WOOD and Dietetic Staff. 2:00–3:30 p.m., Monday, Wednesday and Friday. February 6–March 31, 1939.

MEDICINE CE 7—Practical pharmacology. Fee \$25. Dr. H. T. HYMAN. 2:00–3:00 p.m., Tuesday and Friday.

MEDICINE CE 9 E. C.—Clinical electrocardiography. Fee \$35. Drs. A. M. MASTER, H. L. JAFFE AND S. DACK. 1:00–3:00 p.m., Friday. February 10–April 14, 1939.

MEDICINE CE 10—Diseases of the heart: Clinical features interpreted through roentgenologic, anatomic and histologic findings. Fee \$50. Drs. B. S. OPPENHEIMER, A. M. MASTER, C. K. FRIEDBERG, P. KLEMPERER and Morbid Anatomy Staff. Hours to be arranged. February 10–March 31, 1939.

MEDICINE CE 12—Clinical features of irregular heart action. Fee \$25. Dr. I. R. ROTH. 10:00–11:00 a.m., Monday and Friday. February 6–March 31, 1939.

MEDICINE Ce 14—Diseases of the chest. Fee \$35. Drs. H. NEUHOF, C. B. RABIN, A. S. W. TOUROFF, H. HENNELL AND I. S. SCHAPIRO. 9:00–11:00 a.m., Friday. February 10–May 26, 1939.

MEDICINE Ce 17—General and special pathology. Fee \$40. Drs. P. KLEMPERER AND S. OTANI. Hours to be arranged. February 7–April 14, 1939.

MEDICINE Ce 18—Surgical pathology. Fee \$50. Drs. P. KLEMPERER AND S. OTANI. Hours to be arranged. A ten weeks' course to be given at the conclusion of Medicine Ce-17.

INTENSIVE CARDIOLOGY

MEDICINE Ce 30 Intensive cardiology. Fee \$100. Staff of instructors: Drs. B. S. OPPENHEIMER, M. H. BASS, E. P. BOAS, A. M. FISHBERG, A. M. MASTER, I. R. ROTH, S. H. AVERBUCK, S. DACK, C. K. FRIEDBERG, H. HORN, H. L. JAFFE, H. MANN, S. SILVER AND M. L. SUSSMAN. 9:00 a.m.–5:00 p.m., daily. Probably month of May, 1939.

ENDOCRINOLOGY

ENDOCRINOLOGY Ce 1 Gynecological endocrinology. Laboratory course in bioassay of female and male sex hormones. Fee \$50. Drs. R. T. FRANK, M. A. GOLDBERGER, G. FELSHIN AND E. KLEMPNER. 2–4 p.m., Tuesday and Friday. February 7–March 3, 1939.

GYNECOLOGY

GYNECOLOGY Ce 2—Gynecological pathology. Fee \$60. Drs. S. H. GEIST, J. A. GAINES AND R. I. WALTER. 2–4 p.m., Tuesday and Friday. April 4–May 12, 1939.

NEUROLOGY

NEUROLOGY Ce 1—Applied neuroanatomy and neuropathology. Fee \$100. Dr. J. H. GLOBUS. Hours to be arranged. February 6–April 1, 1939.

OTOLOGY

OTOLOGY Ce 1—Clinical otology. Fee \$60. Drs. J. L. MAYBAUM, W. L. HORN, S. ROSEN, J. G. DRUSS, H. ROSENWASSER, E. R. SNYDER AND J. L. GOLDMAN. 9:30–11:00 a.m., Monday, Wednesday and Friday. 2:00–3:00 p.m., Tuesday; 2:00–4:00 p.m., Wednesday and Saturday, and other hours to be arranged. February 6–April 1, 1939.

OTOLOGY Ce 2—Otologic neurology. Fee \$25. Dr. J. L. MAYBAUM and Staff. 2:00–3:00 p.m., Thursday. February 9–March 16, 1939.

OTOLOGY Ce 3—Otologic histo-pathology. Fee \$35. Dr. J. G. DRUSS. 4:00–6:00 p.m., Tuesday and Friday. February 7–March 10, 1939.

DERMATOLOGY

DERMATOLOGY Ce 1—Dermatology and syphilis. Fee \$35. Drs. I. ROSEN, L. CHARGIN, S. M. PECK AND Staff. 2:00–4:00 p.m., Tuesday, Thursday and Saturday. February 7–April 1, 1939.

DERMATOLOGY Ce 2—Clinical dermatology. Fee \$35. Drs. I. ROSEN, O. L. LEVIN AND M. SCHEER. 2:00–3:00 p.m., Monday, Wednesday and Friday. February 6–March 31, 1939.

PEDIATRICS

DISEASES OF CHILDREN CE 4-E. C. Clinical measurements of intelligence. Fee \$15. Dr. I. S. WILE. 2:00-3:00 p.m., Wednesday. February 8-March 29, 1939.

INTENSIVE GASTROENTEROLOGY

MEDICINE CE 32—Intensive Gastroenterology: Its relation to internal medicine and abdominal surgery. Fee \$100. Drs. B. B. CROHN, A. WINKELSTEIN, P. KLEMPERER, S. J. GOLDFARB, G. BAEHR, B. S. OPPENHEIMER, R. OTTENBERG, R. COLP, J. H. GARLOCK, F. HOLLANDER, H. DOUBILET, S. D. MANHEIM, E. GRANET AND H. YARNIS. 9:00 a.m.-5:00 p.m., daily. Probably month of May, 1939.

For further information concerning the above listed courses, please apply to Miss Edith L. Levy, Secretary for Medical Instruction.

RADIOLOGY*

The following courses in CLINICAL ROENTGENOLOGY will be offered during October, November and December, 1938, and will be repeated during January, February and March, 1939.

Rc 2—Roentgenology of the osseous system. Drs. LEOPOLD JACHES AND MARCY L. SUSSMAN.

Rc 9—Roentgenology of the thorax. Drs. LEOPOLD JACHES AND MARCY L. SUSSMAN.

Rc 10—Roentgenology of the heart and mediastinum. Dr. MARCY L. SUSSMAN.

Rc 11 and 12—Roentgenology of the gastro-intestinal tract. Drs. LEOPOLD JACHES, S. J. GOLDFARB AND MARCY L. SUSSMAN.

Rc 17—Roentgenology of the genito-urinary tract. Drs. LEOPOLD JACHES AND MARCY L. SUSSMAN.

Rc 18—Gross Pathology for Radiologists. Dr. PAUL KLEMPERER

The following courses in RADIOTHERAPY will be offered during April, May and June, 1939:

Rt-2—Principles of radiation therapy. Dr. WILLIAM HARRIS.

Rt-2—Microscopic tumor pathology. Dr. PAUL KLEMPERER.

Rt-2—General principles of skin, intra-oral disease, lower respiratory system, breast, circulatory system and blood-forming organs, bone tumors. Breast neoplasms. Dr. WILLIAM HARRIS.

Rt-2—General principles, head and neck, gastro-intestinal and genito-urinary. Drs. WILLIAM HARRIS, M. GOLAN AND S. RICHMAN.

* These courses are subject to change.

RT-2—Blood dyscrasias, lymphosarcoma infections, etc. Drs. WILLIAM
HARRIS, A. KEAN AND N. ROSENTHAL.
RT-2—Gynecology. Dr. WILLIAM HARRIS.

For further information apply to Dean, School of Medicine, Columbia
University, 630 West 168 Street, New York City

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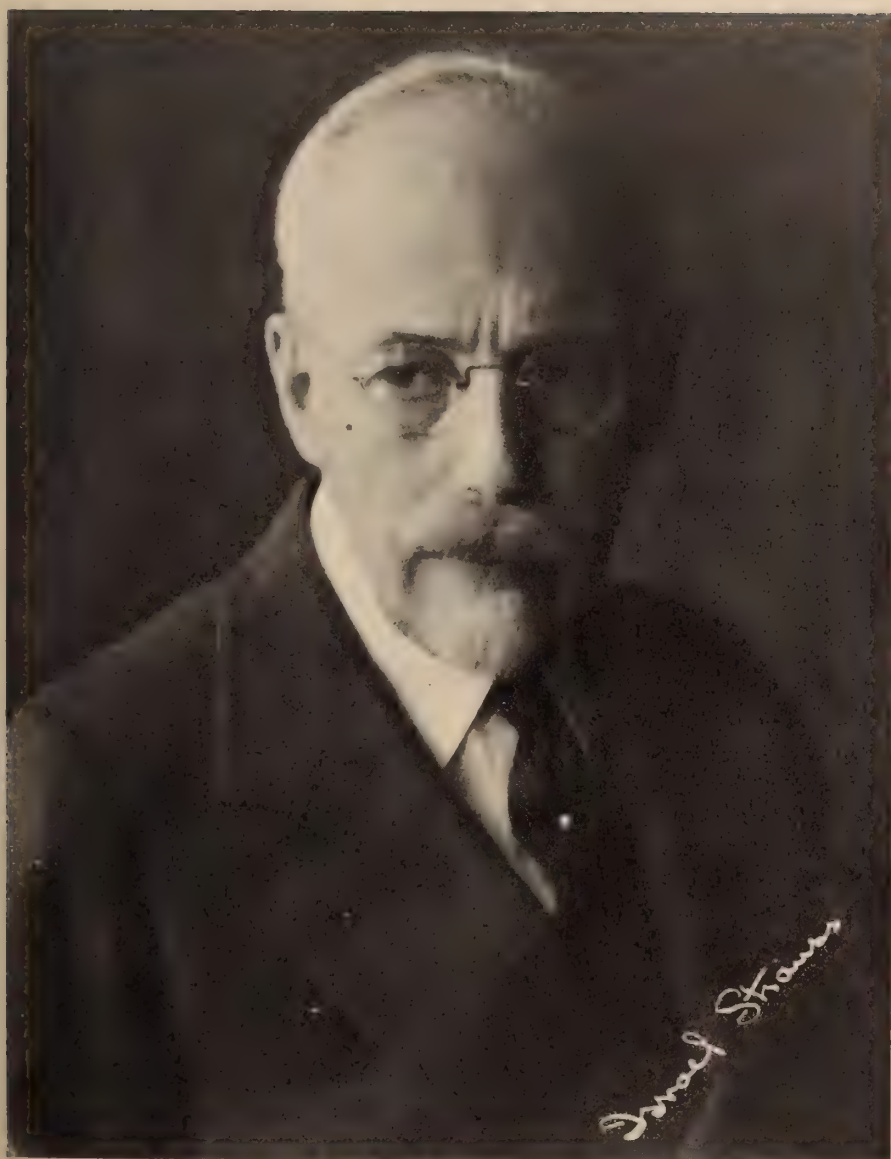
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This special number of the Journal is dedicated to

DR. ISRAEL STRAUSS

to mark his completion of thirty-two years of active
service at The Mount Sinai Hospital.

His friends, colleagues, and pupils join to express,
by means of this volume, their appreciation
and esteem.



NOTES ON CLINICAL OBSERVATIONS AND METHODS

EMANUEL LIBMAN, M.D.

[*New York City*]

My regard and admiration for Israel Strauss have always been so great, that I value the opportunity of contributing something to this volume issued in his honor. After deliberating as to what subject might be most appropriate, I came to the conclusion that I should put down some of the clinical observations that I have accumulated for many years, and the particular methods that I employ for diagnostic purposes. My old and good friend, like Dr. Alexis Carrel and some others, has urged me to do this for a long time, and I know that he will feel happy at my beginning to do so in this volume.

It is my purpose to make these notes as brief as possible, giving details of illustrative cases only when essential. References of anecdotal kind will be added when of sufficient interest or in order to fix points in the reader's memory.

* * * *

PALPATION of the head should be part of every routine physical examination. It is particularly important when searching for metastatic tumors. When I taught undergraduates it was my custom to say that every patient should be examined from the top of the head to the soles of the feet, every opening explored (including hernial rings), and ophthalmoscopy performed. Many years ago, a student following this teaching had the satisfaction of making a correct diagnosis in a case in which no diagnosis had been ventured, but he had also some unhappiness. He wandered into a ward of a hospital, and examining a patient, first palpated the head, and noted two somewhat tender nodular masses in the bones. Realizing that these might be metastatic neoplasms, he palpated the breasts, and in one of them found a mass. When he met the interne in charge of the ward, and asked whether the patient in question might not be suffering from a carcinoma of the breast with cranial metastases, he was told to mind his own business and warned not to enter that ward again.

* * * *

IN 1906 I pointed out that in cases of general staphylococcus infection in children, especially very young children, a crop of small pustules might appear in the scalp, which were large enough to be palpated. Such cases have a very serious prognosis. They may occur with or without the development of an endocarditis. Similar lesions may be encountered elsewhere, one favorite position being over the shins.

IN cases of erysipelas of the scalp, the diagnosis may be missed for several days, or entirely overlooked. Such patients usually complain of pain in the head, have more or less fever, and present tender enlargements of the posterior cervical lymph nodes, on one side or both. It is important, therefore, when examining the head to look for redness of the scalp, and to palpate carefully for swelling and tenderness. It is to be remembered that in erysipelas of the scalp, redness of the skin may be absent during the first few days. This, the so-called white erysipelas, is not infrequently present in the scalp, following upon operative interference in cases of mastoiditis. The condition is then apt to be mistaken for edema, and some other form of wound infection suspected, or sinus thrombosis. Contrary to the experience in sinus thrombosis of otitic origin, blood cultures in these cases of erysipelas nearly always give negative results.

* * * *

IN cases of mastoiditis, tenderness may not be elicited because the patient happens to be hyposensitive, or the cortex is very thick. It is, therefore, necessary not only to test for tenderness in the usual way, but also to make use of fairly heavy percussion with the flexed second and third fingers. The bone should not be rubbed—rubbing of normal periosteum is often painful. I particularly recollect the first case in which I found this procedure of value. The febrile patient had had otitis media and a blood culture had revealed a small number of streptococci. Operative interference had been withheld because of the absence of aural discharge and of mastoid tenderness. By the percussion method I elicited tenderness over the antrum, and at the position of the emissary vein. At operation, pus was found in these two locations, and also a thrombosis of the lateral sinus.

* * * *

It occasionally happens that tenderness of the mastoid process, like that of other bones, is due to a generalized disease. Two cases are vivid in my memory. In the first, following upon an otitis media of short duration, there was a fairly high oscillating temperature and pain in, and tenderness of, the mastoid bone. Fortunately I noted that the patient had the peculiar waxy-yellow color that is seen in cases of leukemia. The sternum was very tender on percussion. Blood examination revealed a leukemia with only moderate increase in the leucocyte count. The other case was still more remarkable. A young woman, with high temperature elevations, complained much of pain behind the right ear, and the bone was very tender. I was requested to make a blood culture. Operative interference was set for the following morning, but during the evening the pain and tenderness disappeared, and there developed an inflammatory lesion of the right upper tibio-fibular joint. Operative interference was not carried out. The blood culture revealed the bacillus of glanders. The question

then arose as to how the infection could have occurred. The occupation of the patient was given as stenographer. On further questioning, it was learned that she was employed by a veterinary surgeon. This case taught us the importance of not only knowing the occupation of a patient, but also where he carries out the occupation. Had the patient described above been properly interrogated when first examined, the possibility of glanders would necessarily have been considered.

* * * *

THAT a disease exists in the first cervical vertebra or in the odontoid process of the second, can often be clinically suspected. The clinical picture was described by Rust, and Leyden called it Rust's disease. This is not a good designation because the picture accompanies a variety of diseases involving the structures named. One could speak of the Rust syndrome, or still better, the Rust symptom. I learned of this diagnostically valuable picture from the description given in Albert's volume dealing with the diagnosis of surgical diseases. Patients presenting this symptom have little or no difficulty in flexion of the head, but cannot turn it from side to side. At times only the turning to one side is markedly inhibited.

In turning of the head, the joint between the atlas and odontoid process is involved. Flexion occurs between the atlas and the back of the head. Rust particularly studied the symptom in cases of tuberculous caries. I at first made use of his observation in the diagnosis of metastatic carcinoma and of myeloma. Later I found that it occurs, in a milder form, in cases of ordinary spondylitis.

These patients are apt to hold the head in their hands when changing from the lying to the sitting position or vice versa. They may continue to support their heads, in both positions. Occasionally a patient grasps his head by the hair, on getting into the sitting position. They fear any sudden movement. For that reason, an anxious expression is continually present, which is rather characteristic.

* * * *

THE disorders of the parotid gland have very interesting relationships. Here I wish to refer to only one of them. I was invited to give an opinion in the case of a woman of about 50 years of age, who had developed parotitis on one day, pancreatitis the following day, and facial erysipelas the third day. Fever was present. I confirmed the diagnosis of pancreatitis by a method which I will describe at another time. The sequence of events was very puzzling, and the picture was at first very unclear to me. It then struck me that if the erysipelas had come first, the case would be understandable. An erysipelas might cause parotitis and pancreatitis. To confirm such a view, it was necessary to prove that the erysipelas began in the throat or nose. That evidence was forthcoming. On careful ques-

tioning I learned that the erysipelas first appeared at the junction of the left nostril and the skin of the face, and that the patient had had a violent inflammation of the throat for four days previously.

Some time later I had confirmatory evidence in another patient. She was a woman of about 40 years of age, who, according to the physician's story, developed acute pancreatitis one day, and erysipelas of the left foot the following day. I confirmed the diagnosis of pancreatitis. There was present an erysipelas involving the dorsal surface of the toes, extending to just beyond the web. With the other case in mind, I expected to find more extensive erysipelas of the plantar surface. I was not disappointed, because it extended almost to the heel. Just behind the middle of the foot there was a cut of which the patient knew, due to stepping on a shell at the beach. The pancreatitis had developed before the erysipelas reached the front of the foot. The patient had been unaware of the erysipelas until it spread forwards, because she suffered no pain. On applying my test, she proved to be hyposensitive to pain.

With the other case in mind, I ventured the prediction that the patient would recover from the pancreatitis without operative interference. One can surmise that the lesion in such cases is a diffuse one, resembling the lesion of cutaneous erysipelas. Is it not possible that some of the cases described as peritonitis in cases of erysipelas, were in reality instances of pancreatitis?

* * * *

THE usual method of palpating the submaxillary salivary glands is not satisfactory. To obtain better results it is of value to place the thumb or the second and third fingers over one gland and with it push all the subjacent structures to the other side, and then palpate the opposite gland.

In far advanced cases of chronic renal disease, one may encounter a remarkable hemorrhagic necrotic inflammation of one or both of the submaxillary glands. The lesion is analogous to that of severe pancreatitis. There may be so much collateral swelling present, particularly if the patient is stuporous and does not evince any pain on local pressure, that edema is incorrectly diagnosed. On the other hand, edema due to the renal condition, may largely obscure the glandular inflammation.

* * * *

SMELLING of the exhaled breath may give valuable information in a variety of conditions besides diabetic acidosis. It is of particular interest in cases of renal and hepatic insufficiency. In the former, the smell is ammoniacal, and in the latter we note a peculiar sweetish odor, which by the uninitiated may be mistaken for that of acetone. The odor due to hepatic insufficiency is frequently present, even in the absence of organic disease of the liver. In cases of valvular disease, in which the liver is congested for a length of time, the odor is usually very distinct, and may

constitute a means of predicting a hemorrhagic tendency or jaundice (the former often coming before the jaundice). The hallitus in cases of acute yellow atrophy of the liver is not infrequently of such a peculiar aromatic and sweet character as to lead one to suspect the presence of this disease.

Before drawing any conclusions from exhaled odors, one must carefully learn what the patient may have taken into his mouth for some time before the examination, whether foods, alcoholic or other beverages, fruit juices, spices, chewing gum, etc. There may be interference also because of the disagreeable odor due to pyorrhea alveolaris. But strange and even amusing as it may sound, by smelling further away from the mouth a "uremic" odor may be detected. Occasionally, even when pyorrhea is not present, there is difficulty because renal and hepatic insufficiency are both present. It may be possible to identify the separate qualities of the two odors by recognizing the smell obtained directly over the mouth as differing from that which is caught at some distance from the mouth. Occasionally one can detect the odor characteristic of the one condition nearby, and the other further away.

* * * *

IN examining the mouth, the buccal mucous membrane should be carefully inspected. Just behind the labial commissures one occasionally observes a group of the so-called buccal sebaceous glands of Lublinski. These are but slightly, if at all, elevated, and are of yellowish color. By artificial light they present a whitish color, and may be mistaken for the buccal lesion (Koplik) of measles.

Further back one sometimes sees a number of small, definitely yellow lesions which are probably lipoid in nature. They do not give rise to symptoms. It must be determined whether or not they have any relationship to the gouty diathesis. There is no connection between this condition and the remarkable disease described by Urbach and his colleagues—lipoidosis of the skin and mucous membranes (lipoidosis cutis et mucosae).

* * * *

IN the search for evidence in favor of a diagnosis of subacute bacterial endocarditis, petechia-like lesions in the oral cavity must be carefully evaluated. It must be remembered that in some individuals, and in certain diseases, they may be produced with ease by traumatism. Petechial lesions near the labial commissures may be due to biting of the mucous membrane, a habit to which not a few individuals are prone. These lesions are apt to result in pigmentation that may be later difficult to evaluate.

* * * *

IN cases of suspected lead intoxication, it is necessary to examine the gums of every tooth, because a lead line need not be present in all of them.

For careful diagnosis, one should use a magnifying glass which will make visible the separate pigmentary deposits in the tips of the papillae, and their location a little below the margin of the gums.

* * * *

IN two cases of pseudo-hemoptysis (so-called hysterical hemoptysis) I have noted that the sanguineous fluid is of a peculiar lavender-pink color which I believe has a value in differential diagnosis. Such pseudo-hemoptysis is usually to be ascribed to voluntary injury to the mucous membrane of the mouth. In another remarkable case, in which the expectorated material surely did not arise in the respiratory passages, an explanation of its origin was not forthcoming. In this patient, the passage of intestinal sand was also noted.

* * * *

A valuable method of diagnosis—now not sufficiently utilized—is digital exploration of the nasopharynx. In cases of carcinoma arising in that situation, one may feel the everted hard margin and at times a central ulceration. In some instances, I have detected the lesion before it was found by direct inspection. One must keep this diagnosis in mind in cases of unexplained pain in the head, paralysis of ocular muscles, enlarged cervical lymph nodes (particularly the posterior group), epistaxis, and metastatic neoplasms in any part of the body.

* * * *

WHEN performing digital exploration of the nasopharynx the finger may carry away evidence of diagnostic value. For example, I once recovered a small piece of membrane that contained numerous streptococci in spreads. The patient suffered from weakness, fever, and pain in the back of the neck. Examination revealed some stiffness of the neck and a definite Kernig symptom. The piece of membrane made the diagnosis clear—a streptococcus membranous inflammation of the nasopharynx. The case became still more interesting. On inspecting the mouth for other possible membranous deposits, I noted a definite dark pigmentation of the buccal mucous membrane, and then looking at the patient more carefully than before, observed some facial pigmentation. Of course, I suspected the presence of Addison's disease. The man insisted upon leaving the hospital, after the fever disappeared. A week later, he died rather suddenly, after what was described as a "weak spell." Postmortem examination revealed tuberculosis of the adrenals. The meningism which accompanied the nasopharyngeal infection is to be explained by the tendency to meningism in the presence of Addison's disease.

* * * *

AT a time when I contemplated becoming a pediatrician, one of the men whose work impressed me greatly was the Russian clinician Filatoff (Filatow). His volume of lectures has been the source of much knowledge

and inspiration for many years afterwards. In his lecture on long-continued fevers in children, one of the causes which he detailed, was infection of adenoids.

Digital exploration of the nasopharynx is invaluable in such cases. Children suffering from infected adenoids may be sick for weeks or months, with fever, enlarged cervical lymph nodes, loss of weight, weakness, marked anemia and other important hematological changes, without a diagnosis being made. Digital exploration may not only reveal the diagnosis but also lead to cure. In such cases, a hard, tender mass is felt, which may fill out the whole vault. By boring into the mass, one may bring about a rapid cure. When recovery results following this procedure, it can be taken for granted that pus was present, even if one does not see it. The bleeding, which in my experience has entailed no risk, may obscure any pus that is liberated.

One of my earliest cases is of so much interest that I will give some notes on it. The patient, a boy of 3½ years, about six weeks before coming under my observation, developed a bilateral otitis media with fever. The discharge stopped within a week. From that time on there were rises of fever, at irregular times, even up to 106°F., preceded by chilliness, and followed by profuse sweating. These attacks occurred every day, or occasionally after intervals of one to three days. There was loss of weight and the hemoglobin dropped to 50 per cent. The blood culture was negative. The leucocyte count was 26,000 with 80 per cent polymorphonuclears. Examination by several otologists revealed no complication of otitis media. When I examined him there were present large lymph nodes on both sides of the neck.

As there was no evidence of a complication of the otitis media, I decided to investigate the nasopharynx, suspecting that infected adenoids had caused the otitis media and might have given rise to the entire clinical picture. This suspicion was strengthened by evidence obtained by careful questioning. I ascertained that the child suffered from gagging, cough, and vomiting since the onset of the whole illness. I inquired carefully into the sequence of these symptoms and learned that gagging was the most frequent one, that cough when present followed gagging, and that vomiting when present followed gagging and cough. This sequence I had observed in cases of obstruction in the nasopharynx. On palpation I found a hard mass, into which I bored. There was some bleeding which did not last long. The temperature dropped that night almost to normal, and from the next day on, the child was afebrile. The hemoglobin rose to 70 per cent within two weeks and the enlarged lymph nodes receded. The child made a complete recovery.

I have not experienced any difficulty in connection with the possible presence of benign or malignant neoplasms of the nasopharynx. Such conditions are rare in children, and besides the differential diagnosis from purulent adenoids should not be very difficult.

RANDOM THOUGHTS CONCERNING ACUTE BRAIN TUMORS AND THEIR SURGICAL TREATMENT

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In a contribution to honor Dr. Strauss and his long period of service at The Mount Sinai Hospital, it is fitting to select a subject with which the name of Strauss will always be connected. The tumor now officially called glioblastoma multiforme, which term is therefore used in this paper, was originally named spongioblastoma multiforme by Globus and Strauss. The writer believes that that name is better than glioblastoma. Moreover, the term "acute brain tumor," which was originally used by Globus and the writer, is still satisfactory in spite of the fact that the clinical symptoms of other types of growth may be of short duration. The frequent suddenness of onset of symptoms and the rapid progress and the profound toxic state in which the individual with a glioblastoma multiforme is so often seen, are striking in, and characteristic of, this type of growth.

Pathological Character. In the classification of the gliomas on a histogenetic basis, the glioblastoma multiforme is placed low in the developmental scale because the type cells of which the tumor is composed are immature spongioblasts in various degrees of differentiation. Glioblastoma multiforme is a most rapidly growing and malignant form of glioma which was once called gliosarcoma. A consideration of the clinical course and the histological character of the growth has led the writer to wonder whether the glioblastoma multiforme is, in fact, a glioma at all or whether it is an intense glial reaction to some unknown noxious agent. The acuteness of onset, the rapid progress, the clinical picture in which so often the patient appears profoundly poisoned and toxic, the histological multiform character of the cells, and the central necrosis surrounded by an area of hyperemia, are similar to what is seen in other parts of the body as the result of reaction of the tissues to a toxic agent. For example, a so-called carbuncle is a lesion due to a staphylococcus infection of the skin, in which there is a central necrosis surrounded by an increased vascularity, and histological studies show that, in the swelling, there are connective tissue cells in every state of differentiation. May it not be, therefore, that the glioblastoma multiforme represents the reaction of the connective tissue of the central nervous system to some foreign and toxic agent?

It is sometimes difficult for the pathologist to reach the conclusion whether or not a given specimen of tumor is to be called a multiform

glioblastoma because small collections of immature spongioblasts may be found in the benign astrocytomas. Is a tumor to be called a glioblastoma multiforme if it contains only one or a few areas in which the type of cells and the alterations of the blood vessels are like those found in the malignant glioma? In general pathology an adenoma which contains only a small area in which the arrangement of cells has the features of carcinoma is called an adenocarcinoma. If the gliomas were classified on a similar principle, a number of tumors which are now called astrocytoma would have to be included in the more malignant forms and should perhaps be called spongioblast-astrocytoma. In some of them recurrence after partial removal has both the histological and the clinical features of a typical glioblastoma multiforme. Contrary to the views expressed by some writers, it seems probable that the recurrence of such a growth with the more malignant characteristics is due to the more rapid growth of the areas of spongioblasts, just as in recurrence of an adenoma with islands of invasive cells (adenocarcinoma), it is the carcinoma cells that form the recurrent growth. This seems more likely than that a dedifferentiation occurs.

However justified the viewpoint may be that some of the growths should be called spongioblast-astrocytoma, this nomenclature would, if adopted, bring only greater confusion than already exists. In the group of one hundred pathologically verified successive cases of glioblastoma multiforme upon which this paper is based, only those cases have been included in which the character and arrangement of the cells and the changes in the blood vessels which are characteristic of acute brain tumor preponderated in all of the microscopic sections of the growth that were made and examined.

The Situation of the Growths. The glioblastoma multiforme may be found in any part of the brain but it is most often encountered in the cerebral hemispheres. In fifty-four of this series of one hundred cases, an autopsy was performed, and in more than one-half of them the tumor was situated in the left, and in about one-third, in the right cerebral hemisphere. In most of the remaining cases both sides of the brain were involved. As shown in Figures 1 and 2, the growth was most often encountered in the posterior half of one cerebral hemisphere. These facts are summarized in Table 1.

Some Clinico-pathological Features. An analysis of the symptoms produced by these growths disclosed the interesting fact that in 15 per cent of the patients there was a history of *convulsive seizures* without other disturbances, which preceded the acute symptoms by one to sixteen years—most often one to three years. The significance of this fact is difficult to evaluate but it suggests that some change in the glia may have long preceded the appearance of actual tumor symptoms. It is interesting to speculate upon the possible occurrence of glial changes for many years

before the appearance of symptoms which are clearly due to the neoplasm. Encephalography is now done with great frequency and, when intracranial disease is suspected, it may be repeated at intervals. During the

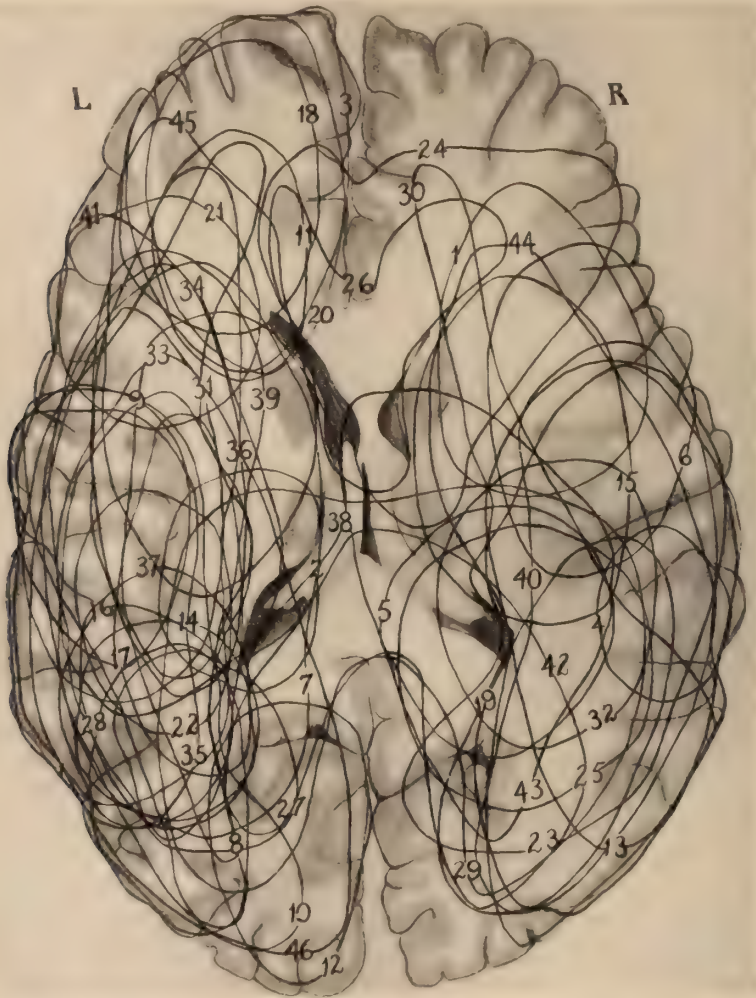


FIG. 1. Showing the position of a group of tumors. The illustration indicates that the majority of the growths are located in the posterior half of the cerebral hemisphere and more frequently on the left side than on the right side. From Elsberg, Davidoff and Brewer: *Journal International de Chirurgie*, 1936.

past five years or so, it has, in our experience, happened a number of times that an encephalogram showed nothing abnormal, but a second one done one or several years later showed clear evidence of a large neoplasm. In the writer's personal experience, this has happened several times in patients

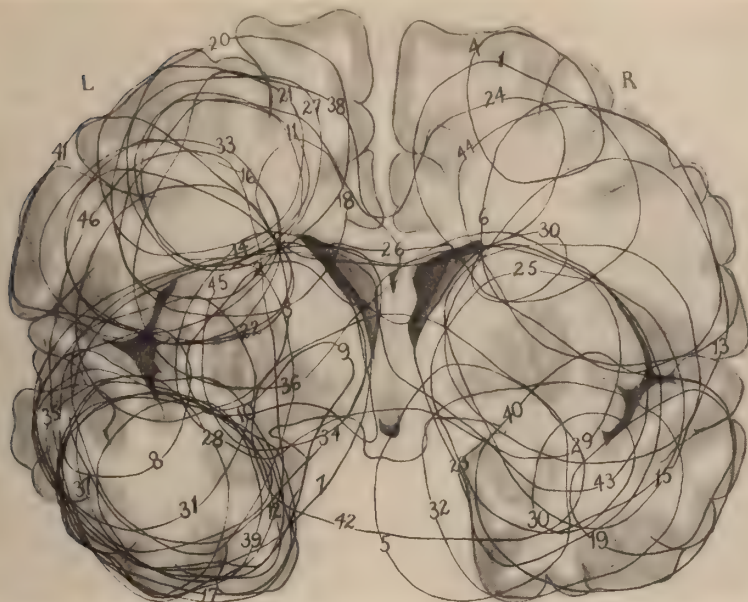


FIG. 2. Showing the position of the tumors in cross section of the brain. Compare with Fig. 1. From Elsberg, Davidoff and Brewer: *Journal International de Chirurgie*, 1936.

TABLE 1
Situation of Tumor at Autopsy

	Number	Per cent
In right cerebral hemisphere.....	18	= 33
In left cerebral hemisphere.....	31	= 56
Bilateral.....	6	= 11
Multiple tumors.....	2	= 3.6

Lobes Involved (in most instances the growth involved several lobes of the brain):

	Right	Left
Frontal.....	10	15
Temporal.....	8	16
Parietal.....	11	13
Occipital.....	4	9

	Number	Per cent
Tumor extended into lateral ventricle.....	7	= 13
Tumor invaded corpus callosum.....	8	= 15
Tumor extended into posterior fossa.....	2	= 3.6
Tumor was entirely subcortical.....	41	= 76
Tumor invaded cortex.....	13	= 24
Tumor contained small or large cysts.....	15	= 27

who had convulsive seizures without other symptoms in whom the neurological examination was entirely negative. One or several years later, on account of persistent or increasing symptoms and of the appearance of objective neurological disturbances, a second air injection was done which showed clear evidence of an expanding lesion within the cranial cavity. It is reasonable to suspect that, in spite of the absence of changes visible on the roentgen films after the first pneumography, the symptoms from which the patient had suffered had been due to a lesion in the same situation as that in which the growth was finally found to be.

In the majority of instances, the *fundus examination* shows a marked papilledema, often with striate hemorrhages. But in a not inconsiderable number of patients, the fundi are normal or show only a slight blurring of the disc margins. In these patients there are no, or only slight, signs of increased intracranial pressure because there is a large area of encephalomalacia which surrounds the tumor mass. When the cortex is not invaded by the growth, the appearance of the brain may easily be taken to be due to a vascular lesion alone, if it were not for the fact that the exposed brain shows more bulging than would occur with a cerebral thrombosis.

Rigidity of the neck and often the Kernig sign are very frequent in patients with a glioblastoma multiforme and occur most often when the tumor has invaded the cortex. The absence of this stiffness of the neck must make one suspect that the growth is entirely, or mostly, subcortical and that there is a large area of softening around the neoplasm.

The intense signs of *increased intracranial pressure* which are more often encountered are, as is well known, due to a considerable degree to the marked swelling or edema of the lobe or hemisphere which harbors the new growth. In the majority of instances, this brain swelling must occur acutely and be responsible for the rapid appearance of drowsiness and stupor. Therefore it is not surprising that in so many instances, roentgenograms of the skull do not show any evidence of the changes characteristic of long existing increased intracranial pressure. It takes at least three to six months for changes to occur in the skull sufficient to be detected on the roentgenogram. This edema of the brain is of considerable significance during surgical procedures. The exposure of the growth is often difficult on account of the marked herniation of the brain when the dura is opened. Furthermore, even though the neoplasm is found to be irremovable, the brain tissue overlying the growth should be incised in order to relieve the brain edema. Our experiences at the operating table have shown us that the immediate postoperative mortality is definitely less when an edematous brain overlying a deeply situated and irremovable growth is incised than when only a decompressive operation has been performed.

Regarding surgical therapy. In large statistics that have been published from various neurosurgical clinics, the multiform glioblastomas formed almost or more than one-half of all intracranial growths, (e.g. Cushing

42.6%, Olivecrona 54.3%, Elsberg 57%) and it is well known that the poor results of the surgical treatment of tumors of the brain in general are due to the relative frequency of the glioblastoma multiforme. The results of statistics from various neurosurgical clinics in the United States, presented at a meeting of the Society of Neurological Surgeons, showed that in the hands of experienced neurosurgeons the operative mortality was high, and that no matter how radical the surgical procedure and how thorough the postoperative roentgen therapy, from 60 to 80 per cent of the patients succumbed within one to two years. In the majority of instances if there was any improvement at all, the relief obtained from the operation was only temporary. Thus, of the one hundred successive cases that were used for this report, 20 per cent of the patients who lived for more than six months were not at all improved; 25 per cent were relieved of their serious symptoms for two to six months; 30 per cent were free from most of their disturbances for varying periods up to ten months; 25 per cent were able to return to their work and to lead an active life for six months up to several years. This summary shows that in the large majority of the patients, surgical interference was palliative.

As the postoperative mortality is high and the results of radical surgical procedures poor, efforts must be made (1) to reduce the number of post-operative fatalities and (2) to devise or discover new therapeutic methods for the glioblastoma multiforme.

1. In eighty-three of the one hundred cases which form the basis of this report, one or more operations were performed. The operative mortality rate (death within four weeks) was 53 per cent. In order to understand the high operative mortality, an analysis was made of the condition of the patient at the time the operation was performed. The operative mortality was lower in those who were in fairly good condition, and if at the time of the surgical interference the patient was in very good general condition, there were no operative fatalities. On the other hand, 90 per cent of the patients who were in stupor and otherwise in poor condition, succumbed within a few weeks of the operation. These figures demonstrate that if the patient is operated upon when he is in stupor, the chances of recovery are small. The appreciation of this fact has recently led me to refuse to operate upon patients in that condition. The patients are treated by thorough dehydration with intravenous injections of hypertonic glucose solution and hypodermic injections of caffein or its derivatives, and are operated upon only if the condition becomes improved. In the majority of the patients so treated, the stupor will yield; in a smaller number, the final outcome is not long delayed. I think one can be certain that those who do not emerge from stupor would, in all probability, have succumbed after any surgical procedure.

Another method which should contribute to the reduction of operative mortality has to do with the management of the increased intracranial

pressure which, in spite of thorough intravenous dehydration both pre-operative and during the surgical procedure, is so often encountered. Not so rarely, although as much fluid as possible has been removed by puncture of the lateral ventricle, in addition to intravenous dehydration therapy, the exposed brain still bulges markedly. If the patient is turned so that the back is sufficiently exposed for a lumbar puncture and after the latter procedure the needle is permitted to remain in place no matter how slowly the cerebrospinal fluid escapes, a marked diminution of intracranial pressure is soon observed and the operative manipulations are thereby simplified. Lumbar puncture during operative procedures, in order to reduce increased intracranial pressure, is not used as often as it deserves.

2. With the appreciation that the results of the surgical treatment of the multiform glioblastoma are poor, the question will arise—what are the advantages of operative interference? Would it be more correct to refuse surgery in many of the patients? In answer: one must acknowledge that,

TABLE 2
Summary of Operative Results Depending upon Type of Operation

	Per cent
Bone flap or decompression:	
Lived up to 1 year.....	18
Partial removal of tumor with decompression:	
Lived up to 1 year.....	10
Lived 1-2 years or more.....	20
Gross total removal of tumor:	
Lived up to 1 year.....	41
Lived 1-2 years or more.....	27

although the preoperative diagnosis of the pathological nature of the neoplasm can usually be made, a more benign and cystic glioma is sometimes found and in rare instances, a patient in whom a multiform glioblastoma seems highly probable, is actually suffering from a remediable lesion—a meningioma or a subdural hematoma. Therefore exploratory operations are usually justified. Whenever possible, the growth should be removed as completely as possible. In the writer's experience, the length of survival is usually, but not always, dependent upon the thoroughness of the operative procedure, as shown in tables 2 and 3.

It is fairly certain that new technical improvements will not contribute much to the results now obtained by the attempts at radical removal of the growths, and therefore, new methods of therapy must be discovered. Efforts have been made to improve radiation therapy.

All of the patients in this series who survived for more than four weeks received x-ray treatment. Whether, and to what extent, the therapy was beneficial is difficult to state, but certainly, in some patients with

recurrent symptoms, roentgen treatment was followed by disappearance of headache and improvement in paralysis. There are so many questions that remain to be answered regarding adequate dosage, the frequency with which treatment should be given, and the methods by which the maximum effect upon the tumor can be obtained, that definite statements regarding the influence of radiotherapy upon the glioblastoma multiforme can not be made. Studies of the effect of the roentgen ray upon the cells and the blood vessels of this type of growth are greatly needed, and more information must be gained of what is to be considered an adequate total dose of roentgenotherapy.

For about one year, with Dr. C. G. Dyke and Dr. L. M. Davidoff, the writer has given single massive doses of radiation (2000 to 3500 r

TABLE 3
Type of Operative Procedure and Survival Periods

OPERATION	NUMBER OF CASES	OPERATIVE FATALITY WITHIN 4 WEEKS OF OPERATION	SURVIVAL UP TO 4 MONTHS	SURVIVAL UP TO 1 YEAR	SURVIVAL UP TO 1-2 YEARS OR MORE
Subtemporal decompression (with removal of specimen or evacuation of cyst fluid).....	12	12	0	0	0
Subtemporal decompression with partial removal of tumor.....	1	1	0	0	0
Subtemporal decompression with grossly total removal of tumor.....	1	1	0	0	0
Flap with decompression (with removal of specimen or evacuation of cyst fluid).....	30	18	4	8	0
Flap—partial removal of tumor.....	16	8	3	2	3
Flap—grossly total removal of tumor.....	19	4	3	6	6
	79	44 = 53%	10 = 12%	16 = 19%	9 = 11%

units) to these growths through the open wound in the operating room. It is far too early to make any definite statements regarding the beneficial or harmful effects of this method. It is already apparent that extended investigations are necessary before the proper dosage, the maximum radiation that normal brain tissue will tolerate, and the effect upon tumor cells of these massive doses can be ascertained. The animal experiments thus far made, demonstrate the interesting fact that the main effect of large doses of radiation is to be found in the nerve cells and myelin sheaths. The effect upon the blood vessels is remarkably slight.

From this random discussion of some features of the acute brain

tumor of the type of the glioblastoma multiforme and its surgical treatment, a conclusion which is not new, is evident: the surgical treatment of this variety of neoplasm leaves much to be desired and new methods of therapy are urgently needed. It is to be hoped that the answer to this, as to so many other problems in the treatment of disease, will sometime be found by a brilliant investigator who will approach the subject from a new and original viewpoint.

NEUROLOGY IN VIENNA, AUSTRIA, AT THE DAWN OF THE PRESENT CENTURY

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Prior to the Great War, Western Europe was the Mecca for votaries of science literature, and music, as well as lovers of fashion and culture in general. Especially popular and attractive were Paris, Vienna and Berlin, and, in the prewar days, it was not unusual to hear English or Russian spoken in some quarters of Berlin or Vienna more frequently than German. In the waiting rooms of such celebrities as Leyden, Nothnagel or Oppenheim one could see patients from such remote countries as India, Egypt and South American republics. The same may be said of the lecture rooms which were crowded with foreign visitors. Aside from the desire to obtain first-hand knowledge and to learn the methods of pursuing original studies, one was also attracted by traditions and the fame of the universities and the prospects of coming in contact with, and getting inspiration from, the famous teachers of the day. The history of the European countries, with their glorious and romantic pasts, monuments, beauty of the country places and cities, great libraries and museums of sciences and arts, were additional attractions. It is, therefore, no wonder that in some laboratories and lecture rooms one could meet representatives of almost every so-called civilized nation.

For instance, in the laboratory of Obersteiner, at the time of my visit in 1901-1902, I met men from Italy, Belgium, Denmark, aside from a number of German-speaking scientists. Even a more diversified group of foreign guests was scattered in the clinical lecture rooms where one could see visitors from South America, Scandinavian and Balkan countries. I myself hailed from Yeniseisk, a northern town in Eastern Siberia, where I had been engaged in general practice for four years following my graduation from one of the then few Imperial Universities in Russia. The province of Yeniseisk, and especially the above-mentioned town was the favorite place for banishment of political "criminals" and "rebels" by the government of the Czars. One of the rebels was the ancestor of Onuf (Onufrowitz), a well known pioneer in American scientific neurology, who was born in the city where I spent four happy years of my life.

The majority of the visitors or guests were from the United States, mainly from the Eastern states and California. Some of the "Americans"

I met subsequently became well known as investigators and teachers. Among them were Howard Rickets, the noted bacteriologist, who was interested in general pathology and neuropathology and who paid short but regular visits to Obersteiner's laboratory; Tarassewich, now professor of neurology in Moscow, was at that time an assistant of Prof. Kojewnikoff, also of Moscow; the late L. Pierce Clark, who in the company of Prout was taking private lessons in neuroanatomy from Marburg, then the young, very active and brilliant assistant of Obersteiner; the boyish looking Irving Spear of Baltimore, who seemed to have had no difficulty in orienting himself in the intricacies and mysteries of neuroanatomy; and a few others. Some of these few drifted to other branches of medicine or preferred the clinical side of neuropsychiatry and were regularly attending the clinical demonstrations. Israel Strauss, for instance, attended Obersteiner's laboratory before me, but was a faithful, though somewhat bored, visitor to the lectures of psychiatry that were given at the Second Psychiatric Clinic of Prof. Wagner v. Jauregg. The Fall course was given by Elzholz, Wagner's senior assistant; the Winter course by Wagner himself. Both Wagner and Elzholz were rather dull lecturers. No attempts were made by them to enliven their lectures by humor or excursions into kindred fields, although the general trend and contents of their lectures were undoubtedly good. Both were faithful disciples of Meynert and never mentioned any contemporary authorities, such as Kraepelin or Krafft-Ebing.

The favorite diagnosis of acute psychosis was, and, as I understand, still is, *amentia* (exhaustion psychosis) and that of chronic or subacute states was *paranoia*, which was diagnosed frequently and liberally. *Dementia praecox* or manic depressive states were never mentioned. A lecture lasted one hour and was divided into two parts. The first half hour was devoted to a didactic outline of the subject and the other half to a clinical demonstration of one or two patients. Very seldom were there ward "walks" by the lecturer and, when such did take place, they were for the purpose of demonstrating how patients were kept, which therapeutic measures were in use (such as emptying a distended bladder by gradual pressure on it) how nasal feeding was to be carried out, or how a catatonic patient was to be handled.

Wagner was already in those days (thirty-seven years ago) deeply interested in febrile treatment of general paresis, for which he advocated inoculation of *erysipelas* as a fever-producing agent. He evidently was not particularly enthusiastic about the *erysipelas* method, for he warned his not very large audience in a monotonous droning voice, without looking at anyone and talking rather into his voluminous mustache, not to be careless or too liberal with this method, lest the state's attorney "get after you." Through Dr. Raimann, one of Wagner's assistants, I obtained Wagner's reprint of an article on fever therapy which he happened to

bring to the lecture room. As Raimann told me afterwards, Wagner was greatly pleased and also surprised to know that a visitor, a pupil of his, should evince interest in his writings, let alone read them. It is the only joke I think he "cracked" in five months of instruction. All this occurred in the Winter of 1902, about fifteen years before he published his famous malaria method of nonspecific treatment of general paresis. Of course, one could learn a great deal from the demonstrations and lectures of this modest, though famous, man, dull and monotonous as they were. The afternoon lectures of some of his assistants were enlivened only by the loud snoring of some of our American friends.

Probably less profound but more "peppy" were the lectures of a contemporary celebrity, Krafft-Ebing. Like Wagner, Krafft-Ebing was of the nobility and highly cultured. Moreover, he was a splendid speaker and because of his oratory attracted large audiences. Unlike Wagner, he was not systematic in his clinical demonstrations which, however, were impressive, thanks to his beautiful German. Like Wagner, Krafft-Ebing ignored Kraepelin's classification and although he recommended, with some reluctance, Kraepelin's textbook he insisted on avoiding its fourth edition. Krafft-Ebing was also officially professor of neurology. In this field he proved less spectacular and even unimpressive. He lacked a sufficient variety of cases, as his clinical material was poor. Year after year, I was told, he would demonstrate the same cases, usually very obscure and therefore wrongly diagnosed and, as in his psychiatric demonstrations, would spend more time on oratory than on actual teaching. In his younger days, Krafft-Ebing probably was a better teacher, but in the days of my attendance he was aged and somewhat handicapped by mild apoplectic strokes from one of which he died soon after I left Vienna (1902). In this connection, I wish to state that the neurologic material for teaching purposes was poor both in quality and quantity. Interesting cases which, as I have pointed out, were demonstrated year after year were often borrowed, the patients having been requested by mail to "show up" at the clinic, often coming from distant places. Viennese material was scattered among the patients of the three medical clinics of Nothnagel, Neusser and Schrötter.

Nothnagel, for instance, occasionally discussed neurologic conditions, mostly of common day occurrence, such as epilepsies and neurosyphilis. Of course, it would hardly be fair to compare the teaching conditions in the Vienna of thirty-seven years ago with those in this country today. That they were at that time better in Europe, especially in Vienna, no one would dispute, but from what I have seen during my subsequent trips to Europe, during the intervening years, the facilities and the material for teaching in this country are to be considered much superior. For instance, at the Chicago Cook County Hospital's neurological out-patient consultation clinics held once a week, there are examined, on the average,

more than one thousand new cases a year, the cases comprising almost every type of neurologic condition, organic and functional. It is quite true that some polyclinics in Vienna were quite crowded by poor wanderers from Russia, the Polish provinces of the then Austro-Hungarian Empire, and other adjacent regions, all of whom hoped against hope to be seen by the professors themselves. But such polyclinics were scarce and not organized for any kind of instruction. For instance, the neurologic department of the polyclinic on Marianengasse near the Allgemeines Krankenhaus was conducted by Prof. Mortiz Benedikt.

Benedikt was an old man of 67 at the time I met him, but he regularly visited his service which consisted of several rooms filled with obsolete electric machines not in use and several wards filled with patients with whom he spent hardly any time. Nor did he show any interest in the dispensary or ambulatory material of his polyclinic, unless the patient exhibited some peculiar anthropologic features, pertaining to the shape of the skull or face. The patients who crowded his clinic were mostly sufferers of anxiety neuroses and were often dismissed with a short remark about the shape of the skull or ear or some slight, peculiar encouragement. Thus an attractive looking woman was once assured that with such a face and body she should not be complaining, for though she has already six children she can produce ("produzieren") a half dozen more. Such psychotherapy was, of course, hardly logical or impressive, at least as far as the patient was concerned.

Benedikt was a prolific writer, bold and outspoken, and an excellent observer, though rather superficial. He did not follow up his ideas or observations by experimental or careful clinical or pathologic work, but, especially in the later years of his life, rather reasoned them out in the calm of his splendid study on Franziskaner Platz. Little as his teachings on such topics as convulsive or epileptic centers or some phases of electrotherapy could be substantiated, he did not hesitate to fight for them, mostly in the form of "open letters" or in international congresses. Like the majority of old men, Benedikt lived in the past and loved to speak of the achievements of his younger days, of his associations and meetings with such men as Griesinger, Skoda, Oppolzer, Zakharin (Moscow) and others. An extremely sociable, kind and clever person, Benedikt often acted as a neglected or unrecognized genius, and for this reason was extremely sarcastic, vain and grumbling. He never failed to inquire of a newcomer what he thought of Benedikt's syndrome "introduced by Charcot" or "paralysis agitans sine agitatione" which he often diagnosed. When in the presence of a new visitor—and I must state here that I was his only pupil who occasionally succeeded in bringing over some friend just to take a look at Benedikt—he would eloquently enlarge on some physiologic theory such as "epileptic" or "spasm" centers. He would carry on the discussion indefinitely, forgetting the waiting patients and the fact that

it was past lunch time. I remember one such incident when I brought over Dr. Modena (then Tamburini's associate in Regio Emilio, Italy) who no longer could stand the strain and loudly complained of "cramps" not in the brain, which Benedikt was discussing, but in his stomach. He never returned. Benedikt was a representative of the old neurology which was based on gross anatomic and pathologic features and, more often than not, on excessive speculations and theoretical discussions.

An equally interesting personality attracted my attention, because he was also neglected and little understood. This was Sigmund Freud. I called on him one evening because my teacher, Professor Darkschewitch (Kazan, Russia), and Freud were old friends, having worked together in the early eighties of the last century in Paris in the laboratory of Charcot. Freud evidently was more interested in another Russian, Professor Gruber, who was a noted anatomist of the nineteenth century and who was a regular contributor to Virchow's *Archiv für pathologische Anatomie*. Each issue of this famous publication contained—for a long period of years—several short contributions by him describing some anatomic anomalies in the human body. Gruber was professor of anatomy in St. Petersburg (now Leningrad) at the former Imperial Military Medical Academy, having been recommended to the Russian authorities by the great Pirogoff. Though he lived in Russia many years he could not master the Russian language, and, as the Russian students could not understand German, he preferred to address them, especially during examinations, in Latin. It is rather hard to comprehend how such a personification of boredom could be a friend of Freud, in whose arms he died in 1885. At the time of my visit to him, Freud was 45, healthy and fine looking, with a black beard and, of course, was extremely kind and friendly. A lonely elderly female was the only other visitor (it was Freud's office hours). I asked him whether he would not be willing to give us a course of lectures on neuroses. To this he readily consented, provided he said, "You could form a small class of at least eight physicians." He grew more enthusiastic when he heard I was not going back to Russia but intended to settle in the United States, in California, as he thought his lectures would be of great help to me in "understanding neurotics so abundant in America." Unfortunately, I was unable to induce even one colleague to join me and I missed the opportunity to be instructed by this great man.

On the whole, neurology was poorly organized in Vienna, regardless of the fact that a number of talented men (Redlich, Schlesinger, and Frankl-Hochwart) were active at that time. But the instructions by these talented men were confined to short courses, of four or six weeks' duration, an altogether inadequate period in which to imbibe knowledge. Clinical neurology was better organized in Berlin, where it was taught by Oppenheim, Jolly and Mendel and their assistants (Cassirer, Flatau, Toby Cohn, Henneberg and others). However, the fundamentals of neurology (es-

pecially neuroanatomy) were much better organized and taught in Vienna. In spite of the unattractive quarters (a very old shack) that sheltered Obersteiner's laboratory, there was a steady stream of applicants for space to either learn the fundamentals of neuroanatomy or to pursue research studies. Crowded as the laboratory was, no one was turned away and systematic instruction was given by Obersteiner himself and Otto Marburg (now of New York), his very gifted, energetic pupil and assistant who ultimately succeeded his famous chief as the head of the laboratory. Not only was normal anatomy gone over, but also some most important pathologic conditions, such as poliomyelitis, multiple sclerosis and syringomyelia were demonstrated, with various staining methods, among which the method of carmine was then especially popular. Neither the anatomic nor the clinical instruction would satisfy a modern laboratory or clinical worker, considering the time and money spent on receiving instruction and traveling, but thirty-seven years ago the teaching was considered ideal and attracted people from all over the world, to both Vienna and Berlin. The departments of internal medicine were even more popular. The clinics of Kowacz, for instance, were in such great demand that it was necessary to register one or more years in advance.

The upheavals that had taken place in the last three decades changed immensely the physiognomy of the Imperial Vienna which was at the height of its fame at the dawn of the present century. During my last two visits there, in 1936 and 1937, it was possible to notice the passing away, the gradual extinction of the glory that once was Vienna. One could see only remnants of the imperial splendor. Wherever one turned—to buildings, shops, parks, palaces, monuments, or to the indifferent, scarce populace on the streets—one could feel that something was missing. One was struck by the atmosphere of helplessness, if not hopelessness, as though an imminent danger was threatening this beautiful historic city and its pleasant inhabitants. The invasion of this peace-loving, small remnant of a formerly mighty and prosperous empire by the Teutonic apostles of liberty and culture, the "saviors of the world from communism," was the realization of the apparently well-founded fears and worry over the fate of this old seat of culture, science and art.

Sic transit gloria mundi!!

EPIDURAL SPINAL INFECTIONS

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When twelve years ago Dandy (1), writing under the title, "Abscesses and Inflammatory Tumors in the Spinal Epidural Space," collected twenty-five cases of abscess, he had none of his own to report. He added three cases of inflammatory tumors (one tuberculous) to seven previously reported. Five of these were probably on a syphilitic or tuberculous basis. The largest group of epidural abscesses personally observed was published by Mixter and Smithwick (2) in 1932. They observed ten cases. Very recently Browder and Meyers (3) reported on seven patients, five of whom had abscesses, and two, inflammatory tumors. Their excellent paper contains a very complete bibliography and a table listing eighty-eight cases, including both the acute abscesses and the granulomas. Since the aforementioned table includes reports from 1855 to 1937, a measure of the comparative infrequency of such infections is at hand. I wish to report on seven cases, five of acute epidural suppuration, and two of granuloma. Neither tuberculous nor syphilitic infection is under discussion.

Etiology. There may be some question of the advisability of considering the more or less chronic granulomas alongside the acute abscesses. They seem, however, to other observers, as well as to myself, to have a common etiology. Infections of the epidural space are considered to occur by direct spread from contiguous structures or by metastasis from a distant focus. When there is a direct invasion from a neighboring infected structure, such as a vertebra or rib, the mechanism is readily understood and is not debatable. In the larger group, which is more important and more difficult to diagnose, the infection arises as a metastasis from a distant lesion, such as a furuncle or an infection of a digit which may have healed and been forgotten before the onset of the spinal symptoms. Many observers have felt that in most instances the infected metastasis is to the epidural spinal fat. Browder and Meyers hold, with some others, that the hematogenous variety most likely always metastasizes to the vertebra, whence it spreads into the epidural space. The evidence they present is very suggestive, especially the post mortem findings of vertebral involvement. As they correctly observe, a small area of osteomyelitis might readily be overlooked on the operating table. Where there is as extensive a bone lesion as is described by these authors, there is every probability that the epidural space was involved secondarily. It is,

however, possible for the vertebra to be invaded from without. The microscopic study of the bone removed in our case 4 suggested this spread, though it does not, of course, rule out an overlooked primary focus in a neighboring vertebra. The stump of a lamina in Browder and Meyers' case 7 was probably secondarily invaded.

Pathology. Once involved, whether from a metastasis to the epidural fat or by spread from a vertebra, the lesion in the epidural space is made up of a varying amount of free pus and granulation tissue. There may be a large quantity of pus extending from the cervical to the lumbar region, and there may be no granulation tissue. On the other hand, the granuloma may be the only evidence of a chronic infection. It may or may not contain droplets of pus; or the combination of considerable granulation tissue and a large amount of free pus may exist. The inflammatory tumors, chronic granulomas, are found beneath the site of a previous skin infection or of a trauma to the back. Where there is free pus only the dura is reddened, though it preserves very often its normal lustre. Where granulations exist they are attached to the dura, on its dorsal and lateral aspects. In the acute cases this attachment is not as intimate as is found in the granulomas where sharp dissection is necessary to free the dura. The fact that there is an actual space between the vertebra and the dura dorsally, allows the pus to spread upward and downward, while the dura itself acts as an effective barrier to the invasion of the subarachnoid space. On the anterior aspect, however, as other observers have pointed out, the dura is intimately attached to the posterior bodies of the vertebra. A large extradural collection of pus is not encountered and perforation into the subarachnoid space is more frequent.

The seriousness of the disease depends upon the extent of the damage to the spinal cord. In the few cases where careful histologic studies of the cord have been reported (Ayer and Viets (4), Hassin (5)), the changes noted have been out of proportion to the pressure of the abscess. There have been noted areas of rarefaction, vacuoles, destruction of fiber tracts and cells. Elsberg (6) explains the findings on the basis of local interference with the circulation of blood in the cord. Browder and Meyers state in their case 3, "Many blood vessels of the cord were thrombosed, being filled with septic thrombi."

Symptoms. In the acute cases the history given by the patients is very uniform. The march of the disease varies but little, and then only in its time elements. The onset is marked by pain in the back. The site of the pain varies with the location of the lesion. If in the case of a rare instance the process is in the cervical region, the pain will be in the back of the neck radiating up to the occiput and down to the arms; if the process is low in the thoraco-lumbar spine, the pain will be low in the back with early radiation down the legs. The most frequent site is in the interscapular region or a little lower, with radiation around to the

anterior part of the chest or upper abdomen. The pain should not be spoken of as just pain, and passed over; it is probably one of the most excruciating pains in the back that a patient can have. It is more or less constantly present and seemingly ever increasing in severity. It is not relieved by the recumbent posture. In fact, many of these patients cannot lie down. Morphine hardly seems to control the agony.

During this period the temperature is usually elevated, but the height to which it goes varies considerably. It may reach 103° to 104° F. or not go above 100° to 101° F. In from a few days to about two weeks neurological signs make their appearance. While the most frequent early complaint is tingling or numbness in the legs, weakness of the legs or bladder disturbances may be the first sign. The rapidity with which the paralysis progresses varies. It may go on to a complete flaccid paraplegia within a few hours (almost minutes) after the onset, or it may take several days to reach this stage. During this time there will be a weakness gradually increasing in one leg, then involving the other. In fact, patients have been reported with a flaccid paralysis of one leg and a spastic paresis of the other. In a very few cases the motor changes may be limited to a foot drop, to a weakness of one leg, or to a spastic paresis of both legs. But the rule is for a rapid progression to the stage of flaccid paraplegia.

An analysis of the time of onset of the neurological signs, from the beginning of pain in the back, was possible in forty-nine reported cases of metastatic abscesses. In fourteen cases the interval was five days or less, in nineteen cases the first neurological sign appeared between the sixth and tenth day, in ten cases between the eleventh and fifteenth day, and in six cases it was over fifteen days. The very short interval in some cases speaks for primary invasion of the epidural space and prompt interference with the vascular supply of the cord.

The sensory findings are not as constant as the motor, though most often there will be found loss of all sensation below the level of the lesion. There are, however, cases in which the motor signs are much more marked than the sensory. At times the sensory level will be found to extend upward from day to day. Early loss of sphincteric control is common. Tenderness over the spine at the site of the lesion is a constant finding.

Two additional observations are of help in arriving at a diagnosis. The white blood count is elevated with an increase in the polymorphonuclear cells. The lumbar puncture yields further information. If a manometric determination is done, there will be block on jugular compression. The fluid is often xanthochromic, though it may be clear. The total protein content is high and there may be, though not necessarily so, a pleocytosis.

More than a word of caution is needed in advocating lumbar puncture. Regardless of the site of origin in the canal of the infection, very many patients will have pus in the epidural lumbar space because of a gravity

abscess. This was encountered in three of my five patients. There then exists the obvious danger of traversing the layer of pus and infecting the subarachnoid space, initiating a meningitis. If the diagnosis be suspected, the stilet should be removed from the needle after the skin has been traversed. In this way pus would be obtained before the dura is reached.

In the granulomas the evolution is less rapid and more closely resembles that of cord compression from a tumor. The pain, while less than in the abscess cases, is much more severe than that seen in spinal cord tumors except some of the giant tumors of the cauda equina.

CASE REPORTS

Case 1. On August 24, 1930 a sixteen year old boy was admitted to the Barnert Hospital. On August 18 a superficial abscess had been incised over the knee. Twenty-four hours later he developed pain in the lower abdomen and chest. Two days later the neck became painful and was held rigidly. The temperature on admission was 104.2°F. The neck was rigid and a positive Kernig sign was noted. The white blood count showed 42,000 cells of which 90 per cent were polymorphonuclear leucocytes. The spinal fluid contained one cell and what appeared to be cocci. Though the culture was negative, antimeningococcus serum was given. Culture of fluid obtained the following day was also negative. On August 26 no fluid was obtained on two attempts. The following day I obtained a few drops of pus in the lumen of the needle introduced into the lumbar region and clear fluid with seventeen cells from the cisterna. There was weakness of the legs, tenderness and fulness over the upper thoracic spine, and X-ray evidence of bone destruction of the arch of the fourth thoracic spine. Laminectomy revealed an abscess in the soft parts, disease of the fourth spinal arch and free pus in the epidural space. The culture yielded staphylococcus aureus. The patient did not improve following this drainage. He was unable to void, though no new neurological signs appeared. On September 3 drainage of the lumbar epidural space was instituted by laminectomy. A blood culture on September 5 yielded staphylococcus aureus in pure culture. The patient died on September 7.

Remarks. This type of epidural abscess was secondary to an osteomyelitis of the vertebra, but was only part of a picture of a general sepsis. In the light of further experience, the necessity of the second laminectomy is questionable, although when it was carried out considerable undrained pus was observed in the lumbar epidural space.

*Case 2.** (Adm. 348583.) On February 1, 1933 a male infant, six months old, was admitted to the pediatric service because of fever of six days duration. The temperature range was from 99° to 103°F. On the day of admission rigidity of the neck was noted. This and a questionable injection of the pharynx were the only abnormal physical findings at the time of admission. A lumbar tap the following day yielded xanthochromic fluid which contained 150 cells. The white blood count showed 15,200 cells, of which 46 per cent were polymorphonuclear neutrophils. Three days

* This case was reported by L. W. Rauh in the Journal of The Mount Sinai Hospital, 1:13, 1934.

later the spinal tap was repeated. At this time only a few drops of xanthochromic fluid were obtained which showed 160 cells, of which 70 per cent were polymorphonuclear in type. On the eighth day after admission a flaccid paralysis of both upper extremities appeared. Two days later a spastic paralysis of the lower extremities began. About this time a swelling was noted to the right of the lumbar vertebrae. Neurosurgical consultation was asked. Pus was obtained from a needle introduced into the epidural region in the third lumbar space, and pressure over the swelling increased the flow. It was felt that this pus represented a gravity abscess from a lesion originating in the cervical region. However, X-ray examination of the cervical spine disclosed no abnormality. An immediate operation was carried out. The pus in the lumbar musculature was found to communicate with the epidural space in the region of the second lumbar vertebra. The spines and laminae of the second and third lumbar vertebrae were removed and pus was seen pouring down from above into the epidural space. A long drainage tube (subsequently shown by X-ray examination to reach the first thoracic vertebra) was inserted epidurally and the wound packed wide open. A culture of the pus was reported to contain a hemolytic streptococcus. Improvement in motor power began six hours after operation and continued until there was normal power in all extremities. Lipiodol was injected into the tube to determine, if possible, the site of the cervical lesion. It reached the seventh cervical vertebra, but nothing abnormal was seen there. The drainage tube was removed six days after the operation. The boy was seen three and a half years later and seemed normal.

Remarks. The origin of this epidural abscess was never determined. All we know is that it probably arose in the cervical and extended to the lumbar region. The surgical procedure, drainage in the lumbar region, while unorthodox, seemed to us to be following the path nature pointed out. In any event, in this instance it was satisfactory. The finding of a hemolytic streptococcus is somewhat unusual, the majority of such abscesses are due to a staphylococcus.

The cervical region is least often involved. Of fifty collected cases of metastatic abscess, only four were in this region.

Case 3. (Adm. 390090). During a month prior to the onset of her illness, this fifteen year old girl had many boils of the face. Two weeks before coming to the hospital she began to have pain in the lower part of the back. At first she continued at school, but the pain kept increasing in severity so that finally she was unable to lie in bed and found most comfort in the standing position. The morning prior to admission there was a rapid onset of paraplegia and loss of ability to void. Fever had not been noted and at the time of admission the temperature was only 99.6°F. Examination showed a flaccid paraplegia with loss of all sensation and absent reflexes below the tenth thoracic segment. The white blood count was elevated to 20,000 with 80 per cent polymorphonuclear leucocytes. A spinal tap yielded faintly xanthochromic fluid containing thirty-seven leucocytes, a total protein of 135 mg. per cent and complete block on manometric determination. A laminectomy was carried out within an hour after we saw her. The spines and laminae of the sixth to the tenth thoracic vertebrae were removed. A thick layer of granulation tissue covered the posterior dura; in addition, there were about 10 c.c. of free thick pus. The latter subsequently grew a staphylococcus aureus. The patient was discharged after a stay of sixty-five days in the hospital without any return of function.

Case 4. (Adm. 398729). As a boy this patient had suffered with osteomyelitis of

many of the long bones and had an osteoarthritis of the hip. He had been well, however, for eight years until two months prior to his present illness when he began to suffer with furuncles over the body. Some of these, as well as recent scars, were present when he came to the hospital. Three days prior to his admission he began to complain of pain in the lower back. The pain increased in severity and was associated with fever. A severe headache developed three hours before admission. At that time he showed a temperature of 102°F. There was tenderness over the twelfth thoracic spine as well as in the left costovertebral angle. The neck was held rigid, a bilateral Kernig sign was present, and a zone of hyperesthesia was noted over the eleventh and twelfth thoracic dermatomes. The white blood count numbered 16,900, of which 86 per cent were polymorphonuclear cells. On admission two diagnoses were considered, a perinephric abscess and an osteomyelitis of the spine. The following morning when I saw him the signs remained the same. A lumbar tap was considered inadvisable, therefore a cisternal tap was done, which yielded cloudy fluid containing 2,000 cells, with 60 per cent polymorphonuclear leucocytes, but no organisms on spread and subsequent culture. An immediate laminectomy from thoracic eleven to lumbar one was carried out. This disclosed pus overlying the dura with little granulation tissue. The operative exposure seemed to reach the limits of the infection. The wound was packed wide open. Although the meningeal signs persisted a few days, convalescence was smooth for three weeks when signs of an abscess in the soft parts of the thigh appeared. This was opened a week later and the patient went on to a complete recovery. The pus from the epidural space grew out a staphylococcus. The bone removed at the time of the laminectomy was reported on by Dr. Klemperer as follows:

"There is a very severe acute purulent inflammation with actual abscess formation on the surface of the endosteal fascia of some of the particles. One can see a purulent inflammatory reaction within the Haversian channels. Within the bone marrow one can also see in places very conspicuous purulent inflammation and an increase of polymorphonuclear leucocytes is notable throughout.

However, there is no evident bone destruction in the interior of the particles. In view of the fact that there is actual abscess formation on the surface, one can hardly understand that the bone would not be severely destroyed, in at least some areas, if this surface reaction would be an extension of the process from the bone to the surface.

For this reason I feel certain that one must conclude that the osteomyelitis is secondary to the inflammation on the surface."

Remarks. In this instance we were fortunate to have a very early case, before the onset of any neurological signs other than meningeal irritation. He was operated upon sixteen hours after he entered the hospital, just four days from the onset of the back pain. This is the earliest diagnosis and operation that we have found recorded. The case reported by Slaughter, Fremont-Smith and Munro (7) was operated upon five days after the onset, after sixty-six hours of observation.

Case 5. (Adm. 401224). Three weeks before the onset of pain in the back an infected finger was incised. The back pain was noted on arising one morning eleven days before admission to the hospital. The day before admission there was loss of power in the legs and inability to void. During this period the patient claimed to have been afebrile and, on coming to the hospital, his temperature was only 99.4°F. He appeared to be ill. There was percussion tenderness over the fourth to sixth

thoracic spines. Very slight power remained at the hips and the left knee. There was a sensory level at the seventh thoracic segment below which sensation was diminished. The deep reflexes were still present in the legs and a Babinski sign was found on the right. The neck was slightly rigid and a bilateral Kernig was noted.

A lumbar puncture was done, care being taken that the stilet was withdrawn before the dura was penetrated. Slightly xanthochromic fluid was obtained which showed a complete block to jugular compression. There were 30 cells, and the total protein was 90 mg. per cent.

Laminectomy of fourth, fifth, and sixth thoracic vertebrae disclosed a large amount of free pus under pressure in the epidural space. The dura was covered with a thick layer of granulation tissue. The wound was packed wide open. The pus grew *staphylococcus albus*.

During the next few days power began to return in the legs, and sensation improved. Ten days after operation the temperature began to rise. At first no cause could be found. Later retention of pus was noted in the wound. At a second operation this was found to come from beneath a rib and subsequent X-ray examinations showed a prevertebral abscess. This was drained by the thoracic service, but the patient succumbed five days later. Post mortem examination revealed multiple pulmonary abscesses and bronchopneumonia as the cause of death.

The next two cases had the type of inflammatory tumor or chronic granuloma.

Case 6. A man in his late sixties was in an automobile accident in February 1930. There was no memory of a direct blow to the spine, though the patient remembered being badly shaken up. Four months later he began to complain of pain in the lower back. The pain was intensified on coughing and sneezing. For six weeks before his admission to Beth David Hospital he noted weakness of the legs, which increased so that he was confined to bed. For four weeks he had difficulty in voiding. When seen in consultation he had almost complete paraplegia with spontaneous flexion contractions. The deep reflexes in the legs were increased and a bilateral Babinski response could be obtained. The sensory level was at about the tenth thoracic segment. The eighth and ninth thoracic vertebrae were sensitive to pressure. There was a complete block on lumbar puncture. Laminectomy the following day disclosed beneath the eighth and ninth thoracic vertebrae a dense mass of tissue encircling the dura on its dorsal and lateral aspects. This could not be separated from the dura bluntly. It was split in the midline and parts removed by sharp dissection. The report of the excised mass was chronic granuloma. There was considerable postoperative improvement so that the patient was able to get around and he had no sphincteric disturbances.

Remarks. The appearance on the operating table was that of an extradural sarcoma, but it was more dense and adherent than is usually seen in that type of tumor. The very clear-cut traumatic history must be considered when possible etiologic factors are discussed, even in the absence of evidence of a direct blow.

Case 7. (Adm. 409313). A forty-four year old man was readmitted to the general surgical service three and a half months after he had been discharged following an operation for a carbuncle of the neck. The infecting organism was a *staphylococcus aureus*. He had a mild diabetes readily controlled by diet. Shortly after he left the hospital he began to complain of pain in the back of the neck radiating up to the

occiput. Flexion and lateral motion of the head and neck were limited by pain. About two weeks before his readmission the pain became aggravated.

On examination, it was noted that flexion of the neck caused shock-like pains in the legs. The power in the right arm was diminished. The deep reflexes in the lower extremities were increased, the right more than the left, and a Babinski response was obtained on the right. Tenderness was present over the spine of the second and third cervical vertebrae, and an indefinite sensory level seemed to be present at the second cervical segment.

The following day the weakness of the right arm was increased. Some weakness appeared in the left arm and there was retention of urine. A lumbar puncture showed a block and the fluid contained 104 mg. of total protein. There were 13,500 white cells of which 86 per cent were polymorphonuclear.

A preoperative diagnosis of granuloma was made and verified by laminectomy. The "tumor" lay on the dorsal and lateral aspects of the dura beneath the first to third cervical vertebrae, and was rather readily peeled from the dura. Dr. Klemperer's report of the excised tissue was:

"Sections of the material submitted show dense almost hyaline connective tissue, one fragment showing an area of calcification. The veins and capillaries are engorged with blood. There is perivascular infiltration with lymphocytes and occasional polynuclear leucocytes and plasma cells extending here and there into the adjacent connective tissue. Connective tissue fragments showing chronic inflammation. No evidence of phlebitis."

A lumbar tap done nine days after the operation showed that there was no longer any block.

COMMENT

Diagnosis. At the onset, in acute abscess cases, the pain in the back, which is the initiating symptom, will give no lead as to the actual condition. Such a pain associated with mild, or even high, fever can be, of course, due to any one of a number of conditions. As the pain continues, however, with ever increasing severity, a suspicion as to the possible underlying pathology will be aroused. If the history of antecedent infection is obtained, and the pain is as low as the lumbar region associated with some tenderness over the muscles in that region, a perinephric abscess may be suspected, as it was in case 4. With the advent of paresis, poliomyelitis will be thought of. In this condition we do not have sensory changes. After the advent of the paralysis a spinal cord tumor will be considered. The finding of xanthochromic fluid and block may further suggest this diagnosis. However, the fever, if present, the leucocytosis, and the rapidity of the progression of the motor signs speak against the usual spinal cord neoplasm. If, as is often found, the paraplegia is a flaccid one, we have additional evidence. While a similarly rapid progression associated with a flaccid paraplegia is sometimes seen in spinal cord tumors, they will usually be found to be metastatic ones. The age group in most cases of acute epidural spinal abscess is against this possibility.

In the chronic granulomas a history of an overlying infection may suggest the pathology of the lesion, as it did in case 7. While a history of a direct trauma would bring up the same question, in most instances the

diagnosis of spinal cord tumor will be made and the pathology disclosed at operation.

Treatment. There is only one treatment for acute epidural spinal abscess, and that is prompt operation. A laminectomy to provide adequate drainage of the infected focus is performed and the wound left wide open. In most cases the removal of the arches from two or three vertebrae will be sufficient. In rare instances a more extensive procedure or a second laminectomy in the lumbar region may prove necessary. In the case of the infant reported above, lumbar drainage was adequate in caring for a cervical lesion.

In the chronic granulomas the indications and treatment are those of spinal cord tumor.

Prognosis. As far as can be determined from reported cases, no instance of epidural spinal abscess has lived, unless operated upon. The outcome of operation can be considered from two aspects: one as to life; the other, as to return of function. If the sepsis continues actively so that the intraspinal abscess is only a part of the picture, the prognosis is that of the sepsis. This was surely the condition in case 1 and probably in case 5. Another possibility, also shown in case 5, is the spread of the infection, even though it was considered adequately drained at the time of the primary operation. A third factor leading to a fatal issue is that found in all cases of complete transverse lesions of the cord. I refer to the respiratory and urinary tract infections and spreading decubitus.

Meningitis as a complication is relatively rare when the dorsal epidural space is involved. The dura offers a real barrier to the spread of the infection into the subarachnoid space. In the rare instances where the lesion is anteriorly placed, meningitis seems to be more frequent.

Functional return will depend on the extent of the damage to the spinal cord before treatment is instituted. In the face of a flaccid paraplegia, such as was seen in case 3, no improvement can be expected. If, fortunately, the diagnosis is made early, as in case 4 the functional result will be perfect. In between these two extremes there are any number of gradations.

SUMMARY

The relationship of acute metastatic epidural abscess and chronic granulomas of the epidural space is discussed.

Five cases of abscess and two instances of granuloma are recorded. Their symptomatology and diagnosis are discussed. The need of prompt recognition and adequate surgical treatment, especially in the abscess cases, is emphasized.

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UNCONTROLLABLE PROSTATIC HEMORRHAGE

AN INDICATION FOR OPERATIVE INTERVENTION

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While hematuria is frequently seen in prostatic hypertrophy, severe hemorrhage is unusual. This complication results in a rapid drop in blood pressure and hemoglobin, with evidences of shock, and is accompanied by severe suprapubic pain and vesical tenesmus, due to distension of the bladder by blood and clots. Although some of these cases may be relieved by the usual conservative measures, others require urgent cystotomy or even primary prostatectomy to control the bleeding. In the past few years, several examples of this type have been encountered. They are presented to show the necessity of active intervention to avert a possible catastrophe.

The chief reason for the predisposition to hemorrhage is the local congestion produced by the enlarging prostate gland. This results from (A) straining of the patient in an effort to empty the bladder; (B) infection accompanying the presence of residual urine; (C) constriction of the intravesical portion of the prostate by the internal sphincter; and (D) compression of the prostatic veins against the outside sheath. Under these circumstances a severe hemorrhage may arise spontaneously, as in the cases reported by Nogues (1) and Perrin (2); or more frequently, following urethral trauma in attempts at catheterization, passage of sounds or cystoscopy. Such instances have been described by Marion (3), Escat (4) and others. Sometimes a severe hemorrhage follows the operation of suprapubic cystostomy and before the prostatic adenomata are enucleated. This type of bleeding may be due to pressure or erosion of the prostatic mucosa by the indwelling suprapubic tube. Cases of this type were encountered by Aumont (5), Heitz-Boyer (6), Vintici and LaRoche (7), Nogues, and Segurolo (8).

The actual lesion which is the site of the hemorrhage is not always definable. Some authors noted superficial ecchymotic and hemorrhagic areas over the surface of the prostate (Marion, Perrin, Thomson-Walker (9)). Others found a ruptured varicose vein responsible (Finney (10), Kretschmer (11), Albarran (12)). In other cases, ulcerations on the surface of the gland were the cause of the bleeding (Vintici and LaRoche, Heitz-Boyer, Shivers (13)). All the enucleated glands were typical benign fibroadenomata of the prostate. Motz (14) found that, microscopically,

the glands that were accompanied by bleeding showed a large number of new capillaries which were engorged with blood, and, in places, their walls were ruptured.

The clinical picture presented by these patients with a severe hemorrhage is very characteristic. At first, they void a grossly bloody urine. As the bleeding continues into the bladder, the patient develops severe suprapubic pain, marked vesical tenesmus and efforts to empty his bladder may cause only a few drops of blood to appear at the urethral meatus. He writhes in agony with a large distended bladder, his color is pale and his skin is clammy. The blood pressure and hemoglobin drop rapidly so that the patient soon presents the typical appearance of "shock." Attempts to empty the bladder through a large catheter and the use of other measures ordinarily employed, fail to stop the bleeding or evacuate the clots completely. It becomes obvious that the patient's bladder must be opened and a blood transfusion be administered to cope with the hemorrhage.

A word of caution must be made in regard to the differential diagnosis. Vintici and LaRoche did a primary prostatectomy in a patient who presented the above clinical picture. The same severity of bleeding recurred after operation and was found to be due to a large renal neoplasm. On one occasion we had to perform a cystotomy on a man who had profuse hematuria. Previous cystoscopy had shown a large prostate and a bladder tumor from which a biopsy was reported "benign papilloma." To our surprise he had a large flat papillary carcinoma which was hidden behind the prostate gland. He made an uneventful recovery.

A number of cases of severe prostatic hemorrhage will cease to bleed after opening the bladder and evacuating the clots. Sometimes the bleeding continues and, despite local tamponade, the only way to control the bleeding is to do a primary prostatectomy and pack the prostatic bed. Ordinarily, one hesitates to do a one-stage prostatectomy except under special conditions. In cases of severe bleeding, one may be forced to do this radical procedure, even though the patient may be in poor condition. Contrary to expectation, the prognosis is apparently good. There are records in the literature of eleven primary prostatectomies for severe bleeding without a mortality (Boyd (15), Adenot (16), Pasteau (17), Michon (18), Thomson-Walker, Vintici and LaRoche, Nogues, Seguroola, Perrin). Likewise, six patients recovered who required urgent removal of the prostate because of bleeding after a previous preliminary cystostomy (Vintici and LaRoche, Nogues, Aumont, Heitz-Boyer, Shivers). It is surprising how these sick patients tolerate radical surgery.

CASE REPORTS

Case 1. Hemorrhage Following Cystoscopy. Suprapubic Cystostomy. Recovery.

A 58 year old man with prostatic symptoms for several years was admitted to the hospital with a bladder distended up to his umbilicus. After having an indwelling catheter for four days he was cystoscoped. Following this procedure, he began to bleed and his bladder filled with blood clots. His hemoglobin dropped from 93

per cent to 76 per cent and his pulse rose to 124 per minute. He showed evidences of "shock". A suprapubic cystostomy was done (Dr. Hyman) and a large number of clots were evacuated from his bladder. Examination then showed no further bleeding, so that his bladder was closed, leaving a suprapubic tube in place. The source of the bleeding could not be seen. He received a 500 c.c. blood transfusion and made an uneventful recovery without further bleeding. Fifteen days later his enlarged prostate was removed.

Case 2. (Adm. 394581). Hemorrhage Following Difficult Catheterization. Suprapubic Cystostomy. Recovery.

A 67 year old man who had had typical prostatic symptoms for several years was admitted to The Mount Sinai Hospital with his bladder distended well above his umbilicus. He was decompressed with an indwelling catheter (urethral), but, twenty-four hours later, this catheter fell out of his bladder. Attempts to replace it were at first unsuccessful but a soft rubber Coudé was finally passed. He began to bleed and presented the typical picture described above. His blood pressure fell from 200 systolic and 102 diastolic to 155 systolic and 70 diastolic and his hemoglobin dropped to 45 per cent. Despite a blood urea nitrogen of 90 mg. per cent, he was transfused and a suprapubic cystostomy was performed (Dr. Hyman). After emptying the bladder, the bleeding ceased spontaneously. He made an uneventful recovery.

Case 3. (Adm. 370365). Hemorrhage Before and After Cystoscopy. Primary Prostatectomy. Recovery.

The patient, aged 64, was admitted to the hospital with a six months' history of recurrent hematuria and urinary frequency. His prostate was considerably enlarged and there were ten ounces of residual, bloody urine in his bladder. Cystoscopy showed a large prostate with the bleeding apparently coming from the left lobe. During the following twenty-four hours he continued to bleed and frequent bladder irrigations were necessary to avoid the accumulation of clots in his bladder. It was therefore decided to open his bladder after first giving the patient a 500 c.c. transfusion.

After opening the bladder (Dr. Hyman), a huge, bulging prostate was seen. There was a constant ooze of blood from both the intravesical and intraurethral portions of the gland which tamponade could not control. The prostate was therefore removed and the prostatic bed packed with gauze. He made an uneventful recovery.

The specimen showed a few hemorrhagic areas over one lobe and, on section, proved to be a fibroadenoma of the prostate.

Case 4. (Adm. 337209). Spontaneous and Persistent Hemorrhage. Primary Prostatectomy. Recovery.

The patient, aged 62, was first admitted to the hospital in 1932 at which time a transurethral resection was performed. In March 1935 he was seen at the office because of hematuria. Cystoscopy showed a large prostate with bleeding from the left lateral lobe. This area was fulgurated.

Six weeks later he was readmitted to the hospital for persistent hematuria. On catheterization, twelve ounces of bloody urine and clots were found in the bladder. Despite an indwelling catheter and irrigations the bleeding continued. Clots would accumulate in the bladder and require frequent evacuation. In the next two days his hemoglobin dropped from 76 per cent to 55 per cent. In view of the persistent bleeding, his bladder was opened (Dr. Hyman).

The bladder was distended with clots. The left lobe of his prostate was very large and projected into the bladder. From its surface there was a persistent ooze of blood which could not be controlled. The prostate was therefore removed and the bed packed with gauze. He made an uneventful recovery, although he required two transfusions of blood because of his anemia.

Case 5. (Adm. 386466). Very Severe Hemorrhage. Primary Prostatectomy. Exitus.

A 76 year old diabetic was first admitted to the hospital November 7, 1935 in hypoglycemic coma and with a bladder distended to the umbilicus. He recovered promptly from the insulin shock and his bladder was decompressed with an indwelling catheter for five days. Following the removal of the catheter he voided well and was allowed to go home.

Three weeks later he was readmitted to the hospital because of dysuria and urinary frequency. On catheterization, he had six ounces of residual urine. His bladder was lavaged with 4 per cent boric acid solution and the catheter was removed. At 6:30 o'clock the next morning, he was found lying in a pool of blood. There was bleeding from the urethral meatus. He was in a moderate degree of shock with a blood pressure of 100 systolic and 60 diastolic and cold, clammy extremities. A continuous drip glucose infusion was immediately administered and two hours later, a transfusion of 500 c.c. of blood was given. A catheter was then inserted into his bladder and about one quart of thick blood was evacuated. The catheter was made indwelling. At one o'clock in the afternoon he was given another transfusion of 500 c.c. of blood.

In view of the persistent bleeding, his bladder was opened (Dr. Hyman). The prostate gland was markedly enlarged, especially the left lobe. There was profuse bleeding from the left lobe which could not be controlled by packings or mattress sutures. Despite the patient's poor condition, it was felt that the only way to control the bleeding was to enucleate the prostatic adenomata. This was readily done and the usual packings were inserted into the prostatic bed.

At the conclusion of the operation he was given a third transfusion of 500 c.c. of blood. His condition, however, became rapidly worse and he died six hours later.

At post mortem examination it was found that the bleeding resulted from a ruptured arteriosclerotic vessel situated near the bladder neck.

Case 6. (Adm. 350898). Hemorrhage Few Hours After Suprapubic Cystostomy. Prostatectomy Followed by Recovery.

A 63 year old doctor was admitted to the hospital March 12, 1933 with a six months' history of symptoms due to prostatism unassociated with hematuria. Five days later, a suprapubic cystostomy was performed by Dr. Edelman. Several hours later, he developed suprapubic pain and passed blood and clots through his suprapubic tube. Despite irrigation, the bleeding continued until that evening, when the bladder filled with clots which could not be evacuated. His bladder was therefore reopened and the clots were evacuated. The bleeding was seen to come from some large varices overlying the prostate and could not be controlled. The prostate was therefore enucleated and the prostatic bed was packed with gauze. He received a transfusion of 1,000 c.c. of blood. The subsequent recovery was entirely smooth and uneventful.

Case 7. (Adm. 387283). Severe Bleeding After Suprapubic Cystostomy. Prostatectomy Resulting in Recovery.

The patient, aged 64 years, was admitted to the hospital in December 1935 with a history of slow stream, urinary frequency, nocturia, and episodes of acute retention during the preceding three years. Examination revealed the presence of a large prostate gland with over five ounces of residual urine. On December 2, 1935 a suprapubic cystostomy was performed by Dr. Beer.

Two days later the patient suddenly began to pass blood per urethram and through the suprapubic tube. Shortly thereafter, the patient went into shock. A mass was palpated suprapubically, and he was in agonizing pain. After removing a suture and one of the small packings a large amount of urine escaped from the wound, as though it had been extravasated. He was given a 500 c.c. blood transfusion.

The following day, December 5, he was still having a bloody drainage. Under gas anesthesia, the suprapubic catheter was removed and a large blood clot, the size of a placenta, was found filling the atonic bladder. This was removed. The bleeding apparently came from the bladder neck. A silk catheter was introduced through the urethra and a heavy silk thread was drawn through. The bladder end of the silk was attached to a thromboplastin soaked packing and the outside end was anchored tautly to the thigh in such a manner as to keep the packing pressed against the bladder neck. He was given a transfusion of 500 c.c. of blood.

The drainage continued to be bloody. On December 7, 1935 he again passed blood clots through the suprapubic tube. His skin was pale and cold. At five o'clock in the morning he was taken to the operating room and the large prostate removed. He was given a third blood transfusion following the operation.

His subsequent course was smooth and he made an uneventful recovery.

SUMMARY

1. Severe hemorrhage of prostatic origin, uncontrollable by the usual methods of treatment, is a rather unusual occurrence, judging from the fact that only twenty-six cases have been reported in the literature.

2. We have collected a series of seven cases of this type observed during the past ten years.

3. In two cases the prostatic hemorrhage followed instrumentation; in five instances the bleeding was spontaneous.

4. All of these cases were subjected to surgery. In two cases a suprapubic cystotomy sufficed to control the bleeding. In five cases an emergency prostatectomy was performed. Despite this drastic procedure, four of the five prostatectomized patients recovered.

5. Prostatectomy should be reserved for those cases in which the bleeding cannot be controlled by packing, fulguration or other methods of treatment.

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VALUE OF THE VESTIBULAR TEST IN NEUROLOGICAL DIAGNOSIS

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The vestibular tests may offer considerable aid in solving certain neurological problems in which intracranial localization is of prime importance. They may be corroboratory in character and serve to confirm data obtained by other studies. Then again, they may supply information which gives direction to otherwise apparently conflicting observations, and on occasions they may be the only finding to point clearly to a solution when all other examinations give vague, inconclusive or negative results. On the other hand, it must be realized that not a few cases are encountered, particularly of lesions in the supratentorial region, in which the vestibular manifestations are insufficient to justify a diagnosis of a definite localization, and yet a lesion is found at operation, having been localized by other means. Even under such circumstances, the vestibular examination is highly useful, since it aids in excluding subtentorial areas of the brain as possible sites of lesions.

In examining the vestibular apparatus the test is applied not only to the internal ear but also to a large portion of the central nervous system. By this form of examination the intactness of the internal ear, the eighth nerve, as well as that of the various afferent pathways and intracranial structures through which these fibers pass, is established. The tests place one in a position to state whether the lesion is peripheral or central, and, if central, where it is probably located. The progress of a lesion involving the vestibular pathways can also be frequently determined by repeated vestibular tests. Occasionally it is possible by these tests to localize the side on which the lesion is present when other methods fail.

In most instances the caloric test is employed instead of the turning test, inasmuch as the information obtained from the former is more accurate and reliable, since each semi-circular canal is tested separately. It should be remembered that the tests are used mainly as an aid in the localization of a lesion and not to determine its nature. Moreover, conclusions or impressions as to localization should be reached independently of the neurological findings. It should also be borne in mind that the vestibular findings elicited by means of the caloric tests are influenced not only by the presence of the lesion itself, but also by the resultant intracranial pressure. Not without importance is the degree of co-

operation received from the patient. Proficiency in the proper evaluation of these tests depends upon the experience of the examiner and can be acquired only by the study of many cases. Standardization of the technique and of the interpretation of the findings is essential. After careful notation of the vestibular findings, analysis should be based on the present day knowledge of the vestibular pathways. The latter is based upon clinical experience, the result of many examinations, and correlative studies of neurologic, operative, and post mortem findings.

The differential diagnosis of a peripheral and central lesion affecting the eighth nerve is based on the recognition of certain general principles and is of importance in localization by means of hearing and vestibular tests.

A peripheral lesion of the labyrinth or of the eighth nerve is suggested by the following findings: In a peripheral lesion all the responses to stimulation are impaired, and conversely the presence of any one normal response suggests a normal labyrinth and an intact peripheral eighth nerve. Spontaneous nystagmus in the vertical plane, either upward or downward, indicates a central lesion. If stimulation produces a "perverted" nystagmus, for example, an oblique or vertical instead of a horizontal nystagmus, then again the lesion is probably central.

If the findings suggest a central location of the lesion, then the next problem is to identify the seat of the lesion more definitely. The facility with which one is able to do this depends in a great measure upon how well one is able to visualize the various pathways constituting the vestibular apparatus. The simplest method of procedure is that of elimination; beginning with the labyrinth, proceeding centrally one considers each structure separately:

1. If good hearing and one or more responses on stimulating the labyrinth are found to be normal, the labyrinth itself and eighth nerve may be considered uninvolved.

2. For information relative to the medulla including the inferior cerebellar peduncle, the responses obtained on stimulating each horizontal canal separately are studied. The test is performed routinely by tilting the head back 60° after douching. If this produces normal horizontal nystagmus and vertigo with normal past-pointing, these structures are probably not involved.

3. To determine the integrity of the pons, the responses obtained from the vertical canals are analyzed. They are tested with the head in the upright position. If this examination shows normal rotary nystagmus with vertigo, past-pointing and falling, it suggests uninvolved pathways in the pons and middle cerebellar peduncles on the side douched.

An evaluation of caloric tests in posterior fossa lesions based on an analysis of forty verified cases was carried out a few years ago in this hospital. Information of considerable value was obtained. Twenty-two

of these cases were verified cerebellar neoplasms. A resumé of the diagnoses, otological and neurological, and their comparison with the operative and post mortem findings showed:

	number of cases
Complete agreement in localization.....	11
Disagreement.....	4
Partial agreement.....	2
Incomplete examination.....	2
Difference as to side of localization.....	2
Otological findings verified--patient not examined by neurologist . . .	1

Four of these cases showed hearing impairment or total loss of hearing, of the nerve type, on the side ipsilateral with the lesion. One of these had total loss of hearing and vestibular function. The localization made by the otologists was an angle neoplasm. The neurological diagnosis, however, was a cerebellar lesion with involvement of the pons. A right cerebellar cyst was found at operation.

The findings on caloric stimulation, characteristic of a posterior fossa lesion with localization in the cerebellum, are:

Diminution or absence of vertigo.

Diminution or absence of past-pointing, or past-pointing in the wrong direction.

Normal nystagmus, unless pressure upon the brain stem causes deviation from the normal, such as spontaneous vertical or oblique nystagmus, or a perverted nystagmus on stimulation.

Normal hearing. Occasionally there may be present, from pressure upon the eighth nerve of a cerebellar neoplasm, hearing impairment of the nerve type.

Spontaneous past-pointing in one direction or, in the absence of spontaneous past-pointing, an inability to produce a reactive past-pointing, is suggestive of a lesion in the cerebellum. On the other hand, when we are able to produce normal past-pointing of each arm in either direction, it is probable that the cerebellum is intact. As in all methods of diagnosis, there are exceptions to this rule, but, in general, the above holds true.

Of the forty cases studied, eighteen were in the so-called extra-cerebellar group (pontine angle and pontine lesions).

The most common symptom in this group was loss of hearing; this occurred in sixteen of the seventeen angle tumors and in fourteen of these it was the earliest complaint; in two others it was preceded by tinnitus. In two, headache was the first symptom noted. Nine patients complained in addition to deafness, of vertigo, headaches, and dimness of vision. Three had attacks of transient blindness. Eleven patients complained of disturbance of gait, weakness or clumsiness. Two complained of speech disturbance and difficulty in swallowing.

A diagnosis of an angle neoplasm when fully developed, based on vestibular and cochlear findings, presents little difficulty. In the earlier stages tinnitus and a partial impairment of hearing of the nerve type with vertigo, not uncommonly is diagnosed Menière's disease. With further changes in the cochlear nerve, especially diminution, and later loss of vestibular function, the diagnosis becomes quite obvious. Since a fair percentage of all brain tumors are cerebello-pontine angle tumors, a method that is so helpful in either localizing them or excluding them from this region, immediately becomes of utmost importance. While it is true that the neurologist can diagnose angle lesions without a vestibular examination, it is equally true that they must wait for the appearance of general clinical phenomena before such a diagnosis can be made. On the other hand, with a vestibular examination, a diagnosis can be made rather early, at a time when operation promises the best results. The number of conditions that could simulate the vestibular phenomena of a cerebello-pontine angle lesion are very few, so that the vestibular tests furnish a most definite means of determining the presence or absence of such a lesion. The following phenomena are usually regarded as characteristic of the findings in cases of angle tumor:

1. On the side of the tumor, a loss or impairment of auditory and vestibular function.
2. On the opposite side, a normal auditory function, normal responses from the horizontal canal, but absence of responses for the vertical canals.

In brief, otologic examination shows a loss of function on both sides except in the cochlea and horizontal canal of the ear opposite the tumor.

In none of the five cases, the group mentioned above, which showed changes on stimulation of the opposite canals, was this finding observed. On other occasions I have been able to demonstrate this finding. Where such a combination of both peripheral and central phenomena exists in the same patient, the lesion is located in all probability in the cerebello-pontine angle. A tumor in this situation destroys the eighth nerve and produces a typical picture of a peripheral lesion on that side, and, in addition, pressure phenomena which manifest themselves by various so-called "central lesion findings" on testing the opposite canals.

The peripheral lesion element of this symptom complex is not difficult to determine, as the patient usually has a total loss of function of the eighth nerve in both branches, or if the hearing is partially retained, the responses from the horizontal and vertical canals on that side will be completely absent, making the evidence of peripheral lesion on that side fairly clear. It is the "central lesion" element of the picture that requires the greatest interpretive skill. None of our cases showed the typical findings on stimulating the opposite canals. There may be variations, as in five of our cases, from this characteristic finding, making the interpre-

tation far more difficult. For instance, the patient's hearing on the unaffected side may not be normal, due to a long standing catarrhal or suppurative process, or perhaps to an old pre-existing eighth nerve or cochlear degeneration. Again, the horizontal canal on that side may respond, but in such a manner as to make it difficult to determine whether or not such a response is impaired as compared to the fully normal response. Cases of this type often exhibit other phenomena indicative of a central lesion, such as a vertical nystagmus, up or down or perverted nystagmus on the unaffected side, or a definite disproportion between eye responses and vertigo. One of our cases showed the presence of a perverted nystagmus on stimulation of the opposite horizontal canal, i.e., vertical nystagmus upwards and downwards following such stimulation. In three there was observed interference with or wrong past-pointing, with either hand on stimulating the opposite canals. Twelve of the cases of angle tumor gave normal responses on stimulating the opposite vertical canals. Careful observation makes it possible to detect in some instances, a definite difference in the activity of the horizontal as compared with the vertical canals.

An isolated loss or marked diminution of responses from the vertical canals on the opposite side, the occurrence of perverted nystagmus on stimulating the opposite horizontal canal, and abnormalities of past-pointing—all of these phenomena appear to be caused by pressure of the tumor upon the brain stem. In a well advanced growth in the angle, abnormalities in past-pointing are frequently observed either in the form of spontaneous past-pointing or an absence or impairment of past-pointing after ear stimulation. Crossed past-pointing was not observed in our cases but has been noted on other occasions—both arms past-point inward or outward.

In addition to those lesions already discussed, the diagnosis of the following lesions may be further clarified by means of vestibular tests:

In supratentorial neoplasms there is often an increased susceptibility to stimulation, resulting in exaggerated nystagmus with a corresponding increase in vertigo and past-pointing. Conjugate deviation of the eyes on vestibular stimulation may suggest the presence of a lesion on the side toward which there is deviation.

Frontal lobe neoplasms with cerebellar signs may occasionally be identified correctly by excluding, by means of the vestibular tests, the posterior fossa as the site of the tumor.

Menière's disease: The vestibular-cochlear findings in this condition in the early stages show no departure from the normal. Repeated vertiginous seizures result in increasing hearing impairment of the nerve type. The hearing impairment in severe cases or those of long duration may be marked, and in some instances almost entirely gone. The vestibular responses show either no changes from the

normal, or, if the condition has lasted for some time, moderate diminution of all responses.

CONCLUSIONS

1. Vestibular tests are of considerable assistance in the diagnosis of brain stem lesions and particularly in the localization of expanding intracranial lesions. They are useful:

In the differential diagnosis of peripheral and central lesions of the eighth nerve;

In the differential diagnosis of an infra- from a supratentorial lesion;

For more definite location of posterior fossa lesions: cerebellum, pons, cerebellar peduncles, pontine angle, etc.;

In the early diagnosis of cerebello-pontine angle neoplasms;

As aids in localization by exclusion;

For the evaluation of Menière's syndrome.

2. To be of value these examinations should be done by none other than those thoroughly trained in the technique and the interpretation of the tests.

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STUDY OF PELVIC PAIN AND HEAD'S ZONES REPRODUCED BY ARTIFICIAL DISTENTION OF LIGATED FALLOPIAN TUBES

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In testing for tubal patency by carbon dioxide gas insufflation, it has been found that the artificial distention of strictured and closed fallopian tubes invariably causes pain in the pelvis which has characteristic radiation. The length of the distended portion proximal to the stricture determines the location and distribution of the pain, which is also diagnostic of the site of tubal obstruction.

In gynecologic practice, the question not infrequently considered when pain is located on the right side is whether one is dealing with appendicular colic or tubal colic due to extrauterine pregnancy, salpingitis or a twisted ovarian cyst. As a differential aid, attempts have been made, since Head described zones of hyperalgesia, to plot out specific areas of cutaneous hypersensitiveness for diseases of the underlying viscera. The results have not led to the practical adoption of the Head's zones because of frequent overlapping of the zones and lack of pathognomonic areas for each of the organs in question.

Recently a special study of skin hyperesthesia in relation to acute salpingitis was undertaken by J. S. Labate (1). He found, in fifty-three cases of acute salpingitis, that 77.3 per cent showed the presence of skin hyperesthesia, while six out of ten cases of mild subacute or chronic salpingitis showed a Head's zone. Despite characteristic findings, Labate concluded that the zones of hyperalgesia should not be relied upon solely in making the diagnosis.

The different results that have been obtained so far are, in part, due to the fact that in a well defined lesion, such as acute salpingitis, there is not only a marked hyperemia and irritation of the pelvic peritoneum, but frequently there is involvement of the ovary and uterus as well. Thus, if the referred pain is projected upon the skin surface, it may very well consist of a pain complex, the component parts of which are contributed by irritation arising from the different structures involved.

For this reason it has seemed advisable to study the viscerosensory reflex by inducing pain in normal, or at least quiescent, fallopian tubes. This can be accomplished by artificially distending them with a harmless gas, such as carbon dioxide, which is routinely employed in the test for tubal patency. Two types of patients are amenable to this study: one,

where sterility is due to closure of the tubes at different points of their lumen, the pathological process having run its course, and non-irritating adhesions are present, or the tubes are sealed over, as in sacosalpinx. In these cases laparotomy observations, besides diagnostic injection of lipiodol or other radiopaque substances, may have been utilized to corroborate the findings obtained by uterine insufflation. In a second group of patients the fallopian tubes have been ligated and severed for purposes of sterilization. In this group the exact site of ligation is definitely known. For the special purpose of the present study, the fallopian tubes in several patients who needed to be sterilized were ligated at different segments. In subsequently testing them for tubal patency, the tubes become distended proximal to the points of ligation, and thus the pain which is momentarily induced by the distention can be observed, both as to its radiation and the possible presence of cutaneous hyperesthesia.

From previous observations on the test for tubal patency in strictured or completely occluded tubes, it was found, in general, that, if both tubes were occluded at the uterine horns, the pain induced by the gas insufflation would be localized to the suprasymphyseal area. If the tubes happened to be strictured at the fimbria, or sealed at this point, the pain would radiate well out to the sides; if the stricture or occlusion was localized at the fimbria on one side, the pain distribution would correspond to that side. Moreover, the extent of the radiation appeared to correspond to the length of the tubal lumen which was capable of being distended, the latter, in turn, being dependent upon the site of tubal obstruction. Observations in this connection did not include a study of the distribution and extent of associated cutaneous hypersensitiveness.

In this present work normal tubes have been ligated at carefully noted symmetrical and asymmetrical points, and observations were made on the subjective complaint of pain by the patient and on the objective distribution of the Head's zones.

The patient's skin over the abdomen and thighs was first tested for normal cutaneous sensitiveness. The uterus was then insufflated with carbon dioxide gas at a slow rate of flow, the intrauterine and intratubal pressure being gradually increased until the distention produced pain. The pressure level was noted and gas was allowed to flow in to the point of tolerance. In carrying out this examination it was necessary to bear in mind that the ligations had to be preserved because the surgically produced strictures can yield at the ligated points to increasing pressure and open the tubes, thus defeating the sterilization effect of the operation. The pain location is noted while the skin is tested for the Head's zone. In making the observations the examiner should withhold reference to the operative data until the Head's zones have been mapped out. The following case is illustrative of the procedure.

B. L. (Adm. 414786), 11/20/37. This patient had a hysterotomy and

ligation of the tubes for purposes of sterilization. The tubes were tied and severed at different points, the left tube at the fimbria, and the right tube near the uterine horn.

The carbon dioxide gas pressure rose to 120 mm. of mercury (Fig. 1), at which point the patient complained of pain in the left lower abdominal quadrant radiating down the anterior surface of the left thigh. This pain was increased during the next four minutes, during which the pressure rose to 150 mm. of mercury, when the insufflation was stopped. The area of hyperalgesia is shown in figure 2. The point of ligation of the left tube is graphically shown in figure 3 (iodochloral injection). The area of hyperalgesia corresponded with the side of the tube which had been ligated at the fimbria. There was no pain radiation on the right side where the

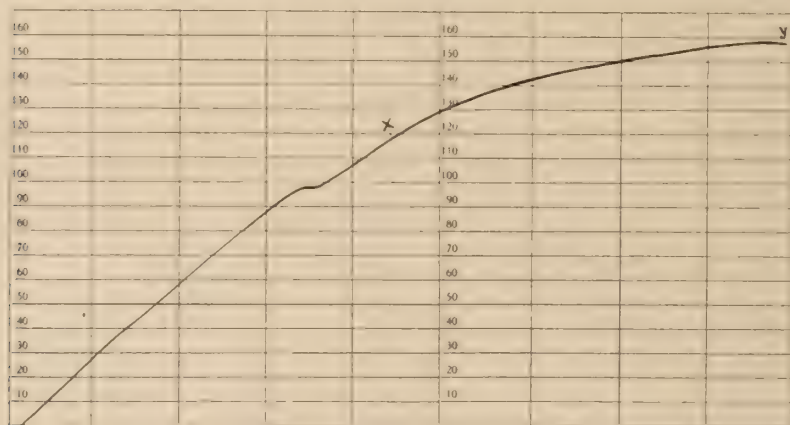


FIG. 1. Kymographic record of insufflation curve, showing duration of test and point X, where pain was first felt by the patient, and continued to Y, at which point the cannula was removed from the uterus when the pain ceased abruptly. (The spaces between the vertical lines represent minutes.)

tube was ligated at the uterine end, nor was cutaneous hyperalgesia elicited on the left side.

These results were reversed when the left tube in another case was ligated at the fimbria and the right tube at the uterine end. The apparatus employed in the test affords us an opportunity of noting how much distention is necessary to cause pain in terms of millimeters of mercury and the volume of gas insufflated; also at what point of the mercury manometer the pain disappears. The latter is accomplished by lowering the pressure very gradually and instructing the patient to state when the pain disappears. The time required for pain to be manifest and disappear can be roughly estimated by repeating the insufflation several times within tolerable limits.

The hyperalgesia has been found, in the cases so far examined by this method, to last for fifteen to twenty minutes, while the disappearance of

the subjective pain is, as a rule, more prompt and coincides almost with the cessation of the insufflation. Whether or not hyperalgesia appears before

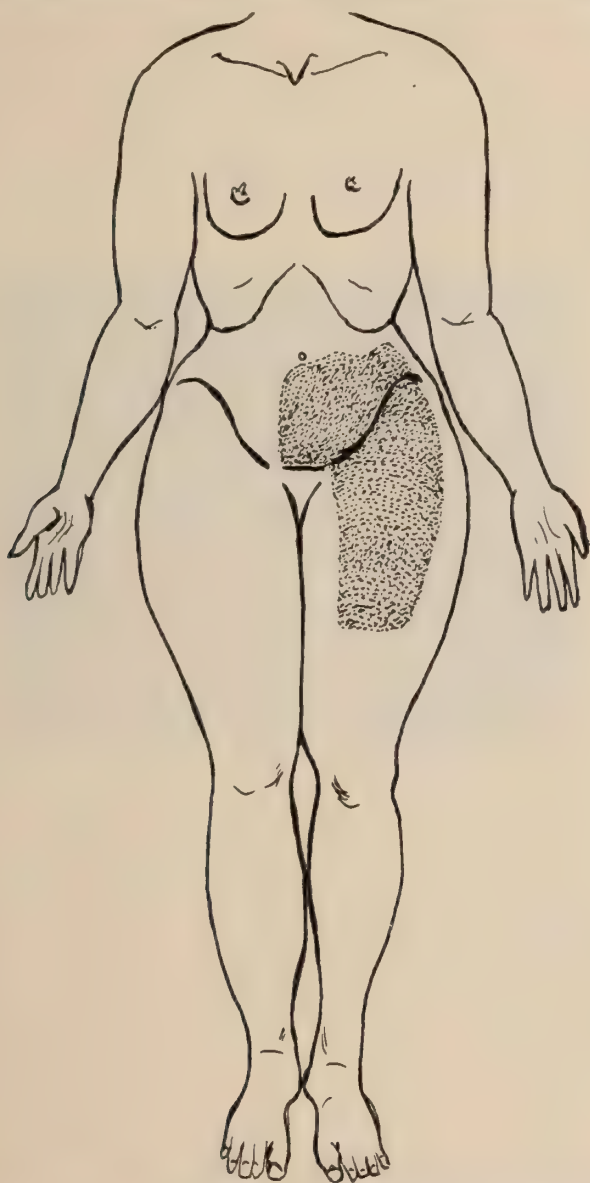


FIG. 2. Area of hyperalgesia in the left lower quadrant of the abdomen and over the anterior central portion of the left thigh.

pain is felt by the patient and as to what extent it persists after the cessation of pain can only be determined by further study in a larger number of cases.

This report is intended only to call attention to a method of studying this particular phase of viscerosensory reflex. The study has not progressed sufficiently for definite conclusions to be drawn. Mapping out the areas of cutaneous hyperalgesia requires training and experience. The patient's ability to interpret objectively the quality and distribution of pain appears to be a factor influencing the plotting of the zones to an appreciable degree, while the method of eliciting the skin hypersensitivity is subject to variability in the hands of the same examiner. Until some entirely objective method is available, which will enable us to record areas of surface hyperalgesia, the estimation and value of Head's zones will

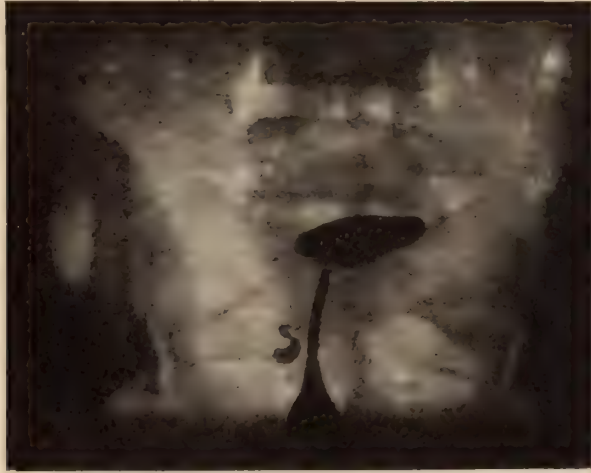


FIG. 3. Iodochloral injection into the uterus and left tube; the shadowgraph extends to the fimbriated end where the tube was previously ligated. The right tubal lumen is not visible owing to its ligation at the uterine end.

be limited. The location and distribution of pain, induced by tubal distention, and indicated by the patient herself, are constant and appear to be fairly typical.

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SUPRASELLAR MENINGIOMA

CASE REPORT

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The subject of suprasellar meningioma has been well covered in the literature by many authors and the pioneer work was contributed, very largely, by Dr. Harvey Cushing. This case is being reported because it demonstrates first, how elusive the diagnosis may be even when it is uncomplicated; second, that vision may be restored and visual fields enlarged after they have been diminished for a long time; third, that careful perimetry and the proper interpretation of the visual fields is of utmost importance; and fourth, that the correct diagnosis will prevent unnecessary operations.

History. On July 9, 1936 the patient, L. K., a female, 51 years old, was referred by her oculist to Dr. Tolstoi for examination. The oculist had been treating her for retrobulbar neuritis. She said that about one year ago, after the menopause, she noticed an increase of weight and, not feeling particularly "peppy" because of this, went to a clinic for treatment. She noticed that vision in the left eye was less acute and was becoming progressively worse. An eye consultant told her this was due to a systemic condition. A general examination was made and several teeth were extracted but to date nothing had been found to account for the reduced vision. There was no history of headache, nausea, vomiting, dizziness, or swooning. She was undergoing anti-obesity treatment including thyroid medication.

Previous history was negative, except that she had been treated for diabetes with insulin. However, for some time she ate what she liked, took no insulin, and was symptom-free.

Physical examination revealed the patient to be a well developed, well nourished adult female, not appearing ill. Cardiovascular, respiratory, and gastrointestinal systems were negative. There was a slight facial weakness, peripheral in type due to a Bell's palsy which occurred ten years before. Urinalysis was normal, spinal fluid, blood Wassermann and Klein tests were negative. The colloidal gold curve was normal. The blood count was normal.

On July 23, 1936 the patient was very much disturbed over the condition of her left eye and sought assurance; she was afraid that the right eye might become involved. She was advised to go on a liberal vitamin diet.

On July 31, 1936 the patient consulted me for the first time. Her complaint was that vision of the left eye had been becoming progressively worse for one year. Examination showed vision of the right eye to be 15/15 with correction, vision in the left eye was 3/200 and could not be improved. Muscle balance was normal. The right fundus was negative; the left fundus showed a nerve head of good pink color though slightly paler than the right, and the arteries were narrower than those in right eye. At the temporal margin of the macula there was a depigmented spot. The tension was normal.

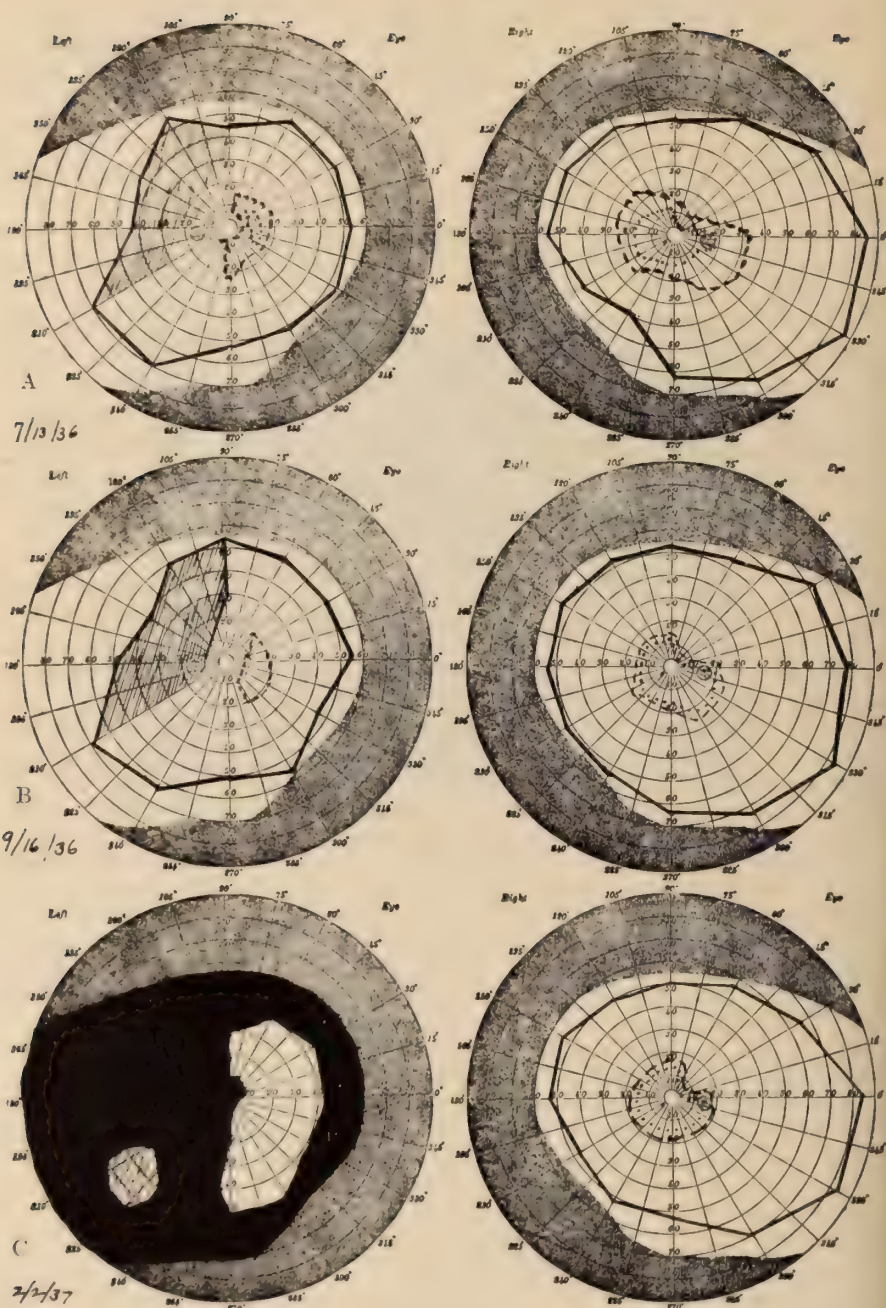


FIG. 1. The interrupted lines represent red. The dotted lines represent green

The visual fields showed a definite tendency to temporal hemianopsia in the left eye and the right eye showed a reduction of the upper temporal quadrant field for color (Fig. 1A). The diagnosis of lesion about the chiasm was made. An X-ray examination that same afternoon was reported by Dr. I. Schwartz to be negative. My diagnosis was suprasellar lesion and I transferred the case to Dr. I. Strauss.

On August 7, 1936 the patient consulted her physician with regard to a proposed tonsillectomy. He thought it inadvisable.

On September 16, 1936 the fields of vision showed a more marked hemianopsia, particularly for color (Fig. 1B).

On October 6, 1936 the patient saw another oculist. From his examination and more X-ray studies he reported: "Mrs. K. has considerable impairment of the visual field of the left eye and there is a suggestion of similar impairment in the right. In my opinion the condition is ocular and I think the manifest involvement of the arteries in the nasal part of the retina accounts for the impairment of the field on the temporal side. I think it is not necessary to assume there is trouble with the hypophysis and it is not likely that paranasal sinus disease is responsible. Mrs. K. says that she has a portion of a tonsil which is infected and I have advised her to have this removed if you approve."

Another internist was consulted and more X-ray pictures taken. He felt that the sinuses should be opened regardless of the fact that they were normal.

Her physician did not agree and the patient wished to consult another oculist. His report was: "We account for this reduction of vision in the left eye by the fact that there is a small scar from a central chorioretinitis. It is true that the optic nerve also looked a little pale. However, the scar to which we have referred would be enough to give a central scotoma. No improvement in this condition can be expected."

On December 12, 1936 the patient was considerably distressed that her eyes were not getting better. General physical examination revealed nothing abnormal.

On February 2, 1937 the patient complained that reading was difficult; she missed the right half of words. For the past few months her oculist was treating her with injections of acetylcholine. It was his impression that she was constantly improving and this was further substantiated by the visual fields which he took. About one week ago there was definite diminution of vision of the right side and the patient became alarmed.

Vision of the right eye was 15/15 with correction; that in the left eye was reduced to recognition of only hand movements. The right pupil reacted promptly, the left very sluggishly. The right fundus was normal. There was pallor of the nasal side of the left nerve head. The fields showed considerable advancement of the hemianopsia and complete loss of the color fields in the left eye and slightly more reduction of the color fields in the right eye (Fig. 1C). I insisted that surgery was imperative. Dr. Strauss concurred and suggested encephalography.

On February 13, 1937 the patient was seen by Dr. Davidoff who also believed that there was a suprasellar cyst (probably meningioma) and advised an encephalography. This was done by Dr. Dyke at the Neurological Institute. It showed the ventral portion of the cisterna interpeduncularis to be less forward than usual with absence of a definite concavity in the rostral region. The ventricular system appeared normal. The findings suggested a suprasellar tumor.

Operation (Dr. Davidoff). A right frontal craniotomy of the Frazier type was performed under avertin-local anesthesia with gross removal of a suprasellar meningioma.

The tumor was an hemangioblastic meningioma about 1 cm. in diameter, originating from the anterior portion of the sellar diaphragm between the legs of the chiasm. The patient stood the operation well and the course was uneventful.

On March 16, 1937 Dr. Davidoff reported that the patient was perfectly well. Her visual fields were very much improved.

On April 7, 1937 vision in the right eye was 15/15 with correction; in the left, 15/30 ++ with correction. The right fundus was negative; in the left there was definite pallor on the nasal side of the nerve head and there was slight pallor in the temporal part. The arteries were narrow, particularly on the nasal side. The visual fields showed marked improvement (Fig. 2A). The most recent fields were taken on July 26, 1937 (Fig. 2B).

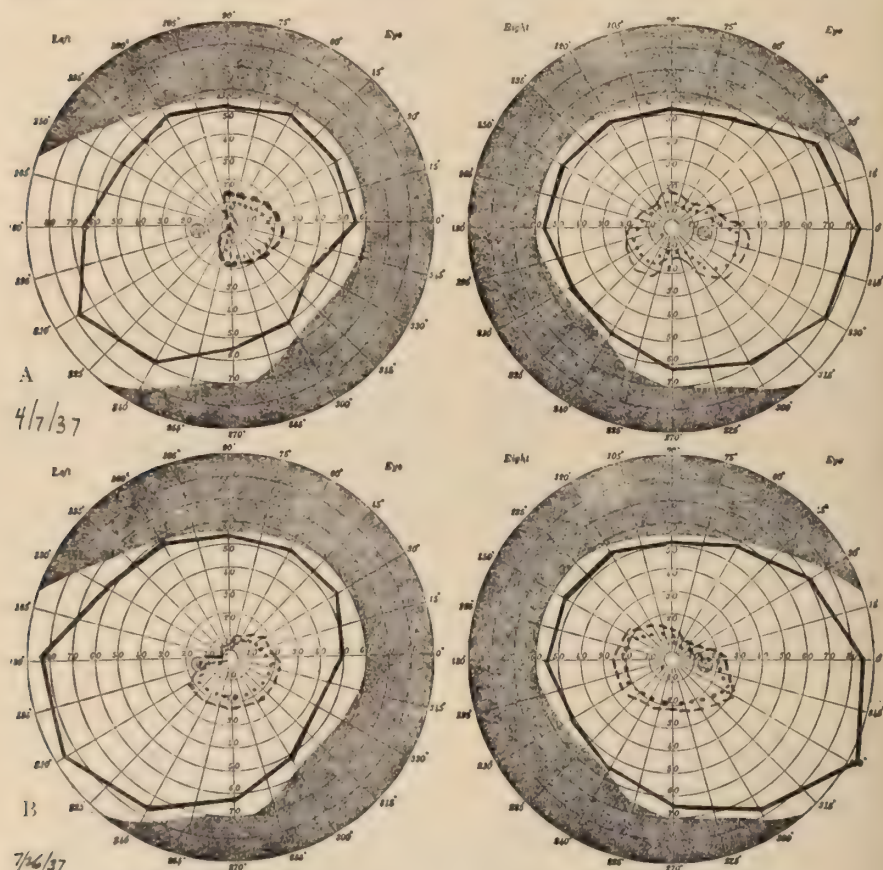


FIG. 2. The interrupted lines represent red. The dotted lines represent green

COMMENT

Suprasellar tumors are not uncommon in middle aged patients. They complain of slowly progressive loss of vision and naturally consult the oculist first. In some cases, where central vision becomes involved, the patient describes the loss of vision as sudden. There is primary optic atrophy. There are no endocrine disturbances and X-ray examination of the skull is negative, except for slight changes late in the course. The possibility of one eye being involved for some time before the other reveals

any signs should be borne in mind so as not to diagnose the case erroneously as one of retrobulbar neuritis (1). Early diagnosis offers an opportunity for successful operation. When the tumor becomes large it may envelop neighboring vessels and render complete removal impossible or dangerous.

While, in general, it is not good to rely on one sign for diagnosis and prognosis, in most cases of suprasellar tumor field changes may constitute the only sign. Almost without exception the field changes are so typical that they definitely indicate involvement of the chiasm. The changes always affect both fields, though always in different degrees, so that the changes in one field are more advanced than in the other. The disparity may be slight or so extreme that one field appears almost blind while the changes in the other may be so slight as to escape observation unless examination is very thorough. The early affection of one field alone is often due to the lesion being at or near the junction of the chiasm with the nerve, rather than involving the body of the chiasm. In many cases a single field will be found sufficient, not infrequently more than one examination is required; sometimes a series may be necessary. Color defects may be found to precede the field changes with white objects. Color testing has the advantage that a delicate test is provided with comparatively large objects. "Color testing cannot be replaced by the use of small visual angles with white" (2).

The early disturbance of central vision is probably the reason why many of these cases are at first treated for retrobulbar neuritis and the patients subjected to operations by the rhinologist, dentist and others. Careful perimetry should eliminate this error.

X-ray examination in suprasellar meningioma is generally negative. In some cases there are slight changes, flattening of the sella turcica or absorption or atrophy of the anterior clinoids. Some show thickening about the base of the anterior clinoids, suggesting that the bone has been infiltrated by the growth beneath its point of origin (1).

All tumors do not arise from the same point of the meninges but one symptom is common to all and essential in explaining the group of symptoms they produce. It is that they are primarily situated in front of the chiasm and that they are eventually straddled by the chiasm (3).

The visual field defects are produced by venous congestion and arterial ischemia rather than by compression of the nerve fibers. Removal of the pressure is followed by rapid recovery unless it has lasted too long.

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EPHEDRINE IN THE TREATMENT OF AUTONOMIC PETIT MAL CONVULSIVE SEIZURES¹

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It is a well known fact that the treatment of convulsive seizures often taxes the ingenuity as a therapist of even the most skilled neurologist. This is particularly true in cases of undetermined etiology wherein the diagnosis of idiopathic epilepsy is reluctantly made. The same difficulty sometimes arises when there is persistence of seizures after the cause is ascertained and even removed. We rely then, in the main, on sedative medication, more particularly on the bromides and phenobarbital. But even here one is often at a loss to explain why in apparently similar cases the phenobarbital is effective in some and not in others, or at one time and not at another. Clinical observation teaches indeed that the bromides are more effective in petit mal seizures and phenobarbital in convulsions, but even this does not always hold.

There are instances where despite persistent and adequate treatment with sedatives, restriction of fluids and attention to diets, there is not only no cessation of seizures but actual increase in their severity and frequency. It is in these cases that persistent search for causes and intensive study of individual factors sometimes bring reward. Occasionally one finds allergic factors, sometimes an endocrine disturbance, rarely a hypoglycemia or an adenoma of the pancreas. Accurate history-taking and meticulous clinical observation often serve as clues. Thus attention to the fact that the seizures were atypical and occurred in one case early in the morning and in another before dinner led to the suspicion of hypoglycemia in the one and adenoma of the pancreas in the other, diagnoses which were subsequently confirmed by appropriate study. Sometimes the very bizarre nature of the grand or petit mal attack or the postural variations before, during and after the fit or the presence of features which are not ordinarily expected and therefore are overlooked, serve as clues both in diagnosis and treatment. It is this careful and prolonged study of the variations in the seizures and detailed analysis of everything pertaining to them that has led to the conclusion that there are epilepsies of varying etiology and that there is no epilepsy as a single entity. Even

¹ Read at the Combined Meeting of the New York Neurological Society and the Section of Neurology and Psychiatry of the New York Academy of Medicine, March 1, 1938.

the fit itself, which is the most consistent manifestation of all the epilepsies, is not uniform and therefore is not always the expression of the same type of discharge from the brain.

This is not the place to enter into a discussion of the nature of convulsive brain discharges and their correlation with the various parts of the brain whence they seem to originate. Suffice to repeat, what every neurologist knows, that seizures often show features which betray their site of origin, and that not all of them are primarily cortical. This is true as much of the grand as of the petit mal seizures. What is pertinent to our discussion is the fact that some fits show features which reflect dysfunction of the hypothalamic vegetative centers. Not all resemble the fits described by Penfield as diencephalic autonomic epilepsy, but they are in the main characterized by vegetative nervous system phenomena and by preservation, at least in the beginning, of consciousness. The following two cases, I believe, fall into this group. They are of interest because of their uniqueness and because of their therapeutic response to a drug which seems to affect the interbrain.

CASE REPORTS

Case 1. Mrs. D., a middle-aged married woman, was first seen by me in August 1937. At that time she complained of spells which she had been having for months. They occurred innumerable times a day, sometimes as many as thirty or forty or more. The spells lasted anywhere from a few seconds to as long as half an hour. Generally they were very brief. They began with a feeling of apprehension, generalized weakness, and fleeting loss of orientation, as if everything were disappearing from under her. She would become very pale and complain of palpitation. Her blood pressure was generally low, about 90 systolic. The pulse, which normally was 80 to 90 per minute, would rise during the spells to 120 and up to 150. With the cessation of the spells she would return to her normal condition.

The history is that on December 17, 1936, she fell out of a speeding car and landed on a cement road. She was unconscious and taken to a hospital where she remained several days. There it was found that she had sustained a right-sided fracture of the skull. Six days after the injury she began to complain of numbness of the left side of the body and suddenly lost consciousness. First the left side of the face began to twitch, then the left arm and leg, and finally the convulsion became generalized. The convulsions kept up two hours, with interruptions. Stupor lasting six hours followed. She gradually improved, but the minor attacks began to make their appearance. On July 7, 1937, while riding in a car, she lost consciousness and had a convulsion, in which the left side was mainly involved. The attack lasted ten minutes. The minor spells, which were regarded as petit mal, increased in frequency. She received phenobarbital and bromides, but neither had any effect on the petit mal attacks.

The description of the numerous spells gave me the impression that we were dealing with a paroxysmal vegetative nervous system disorder as part of the convulsive state. The sudden pallor, the weakness, the rapid pulse, the low blood pressure, and the absence of true loss of consciousness suggested disturbance of hypothalamic function. The attacks were not quite of the diencephalic autonomic type of epilepsy, but possessed sufficient ear-marks to suggest the analogy. Nor did they resemble narcoleptic attacks occasionally seen in chronic encephalitis, and

rarely following brain injury in skull fracture. Nevertheless the thought suggested itself that ephedrine sulphate might be useful, particularly in view of the fact that the medication used hitherto, namely, phenobarbital and bromides, had been ineffective. Wherefore I ordered all drugs discontinued and prescribed ephedrine, three-eighths of a grain to be taken twice daily. The attacks promptly ceased and have not returned, despite the fact that she continued taking the ephedrine only for four weeks. Although the bromides had no effect on the spells, I advised small doses, which she is now taking daily. The patient is entirely well, is no longer afraid to leave the house for fear of the seizures, and has had no grand or petit mal attacks since she has come under my observation.

Case 2. Mrs. T. B., a very intelligent young woman of twenty-four, whom I first saw on July 22, 1937, had been suffering from convulsive seizures and innumerable peculiar spells by day and night for about one year. The diurnal seizures differed in some measure from the nocturnal ones. The former occurred every time she lay down, and particularly when she wanted to fall asleep, the latter kept her awake in bed for most of the night. They occurred at the rate of ten to twenty a day, and somewhat fewer during the night. She was completely incapacitated by them and had to give up her occupation.

The history was that she had been perfectly well up to August 1936, about six months after her marriage. At the age of six she was in an automobile accident which resulted in unconsciousness but was not followed either by immediate or remote sequellae. In February 1936 she had the "flu" and a tonsillectomy. Menstruation, which previously had been normal, became irregular with the onset of the illness, and the libido had diminished.

At first she had spells which were characterized by a feeling of light-headedness, fearfulness, crying out for help, a sensation of being drawn to the floor, and bizarre clonic movements. There was no unconsciousness, no tongue-biting, no incontinence. She was admitted to the Neurological Institute in April, 1937, where neurological examination was entirely negative, as were all laboratory tests, including X-ray examination of the skull, except for a basal metabolic rate of minus twenty-one. Because of the presence of certain psychogenic factors, the diagnosis of conversion hysteria and convulsions was made.

She was readmitted to the Institute on June 16, 1937. She continued to have the spells despite medication: in fact, those at night increased in frequency, up to a dozen or more, each lasting one to two minutes, followed by marked fatigue and characterized by pallor. On May 21, she had a major convulsion at seven in the morning, with tongue-biting and complete amnesia. The attack lasted ten minutes. The next morning she had a similar attack ushered in by a cry. On the night of June 9 her husband awakened to find her unconscious, frothing some at the mouth, the pupils dilated. She evidently had had a convulsion, her tongue being bitten. She "came to" in fifteen minutes. She had another convulsion four nights later. All were followed by complete amnesia.

Reexamination at the hospital was again negative. The blood and spinal fluid were normal and the serology was negative. Blood chemistry was normal. The basal metabolic rate was minus thirty-one. An encephalogram showed some left cerebral hypoplasia or atrophy. The diagnosis this time was idiopathic epilepsy, grand and petit mal. She was given the usual medication of bromide and phenobarbital and thyroid extract. She did not improve; in fact, she grew worse.

More detailed inquiry into the character of the minor spells when I first saw Mrs. B. showed that they consisted of sudden onset of rigidity, at times resulting in falling and getting hurt. There never was unconsciousness during these attacks.

Always there was waxy pallor and a rise in pulse. Occasionally there was tremor. The blood pressure was low—100 systolic and 60 diastolic. These attacks occurred at all times of the day, generally in the afternoon and evening, as many as ten or twenty during waking hours. They were most apt to come on when she would lie down because of fatigue and a desire to relax and to sleep. Their frequency prevented her from working and even from going out. The night attacks, which were almost as numerous, were very much more severe. They would also be accompanied by pallor and rapid pulse, but not infrequently by unconsciousness. At times there were convulsions with tongue-biting. Occasionally she would be roused out of sleep by the muscular spasm. Always both during the diurnal and nocturnal spells the legs and arms would become rigid and extended, the body would bend forward so that the limbs and trunk made a U-shaped figure. The night attacks would set in immediately on going to bed, and so she would try to retire late, about midnight. They were most frequent from the hour of retiring to four or five in the morning when she would fall asleep exhausted and sleep until late in the morning, not however without having some attacks during her sleep. She would arise at ten or eleven, feeling tired and thus prepared, as it were, for the diurnal spells because of the desire to lie down or relax in sleep. The spells gave rise to a vicious circle which brought other spells in its revolutions.

Neurological examination at this time was again negative. It was clear from the history and the description of the attacks that the patient was suffering from both grand and petit mal seizures, but there were features of the minor spells which suggested disturbances of diencephalic function. Among them was the severe pallor, the weakness, the rapid pulse and the low blood pressure. These were not the features of the diencephalic autonomic epilepsy described by Penfield, but there was some resemblance; in fact, they were reminiscent of that syndrome quite as much by their divergence as by their similarity. There was also something suggestive of narcolepsy, if not of cataplexy. Here the resemblance was even more remote, but it was sufficient to raise the suspicion that what passed for the "flu" in February, 1936 may have been an attack of encephalitis. The occurrence of true convulsions, some of which had the features of decerebrate rigidity, which is so rare in chronic encephalitis, naturally pointed away from this etiology. Nonetheless the use of ephedrine suggested itself.

The patient had been taking bromides, phenobarbital, amytal, sugar, and thyroid. These were discontinued, and she was given three-eighths of a grain of ephedrine twice daily and three-fourths of a grain on retiring, together with one dose of a grain and a half of phenobarbital. She returned within a week with the report that the diurnal attacks had decreased from as many as twenty to three or four. These few were milder, were not preceded by the distressing and peculiar feelings, and lasted not more than thirty seconds. The night attacks, though not fewer, were also milder. After another week the report was that the night attacks, too, had decreased and those by day reduced to two. Libido had returned. Within the third week the spells by day had ceased. For several weeks she was free from daily attacks and the ones at night continued to be milder. The ephedrine was continued by day and benzedrine substituted at night. The effect of the latter was not so good. She resumed the ephedrine and the night spells grew milder for a time, but never ceased. She got so well that she resumed her work, which is an important full-time position, requiring long travelling by subway. Previously she would not have trusted herself to go unescorted even to the corner store. On the night of October 2, when she had not taken the ephedrine and the phenobarbital, she had a grand mal attack with unconsciousness, incontinence and tongue-biting.

To date she has been practically free from attacks by day. Those at night vary:

sometimes they are fewer and milder, at other times more frequent and more severe. She is working at her job. She had one or two spells of unconsciousness. Epsom salts, hyoscin, and quinine were tried on various occasions. They were ineffective, and ephedrine had to be given again. She is now taking it regularly. The best dose for her is the one first given, namely, three-eighths of a grain twice during the day and three-quarters of a grain once at bed time. The drug does not seem to interfere with sleep.

COMMENT

As has already been pointed out, the two cases just described did not closely resemble the one reported by Penfield.² To begin with he was dealing with a tumor of the third ventricle which pressed on the hypothalamus. Those seizures were characterized by flushing, perspiration and salivation; all three features were absent in my cases. Pupillary dilatation did occur at times. In both there was increase of pulse rate. Whereas Penfield's case showed an initial rise of blood pressure with a fall only toward the end, the pressure in my two cases was consistently low. The pallor may be looked upon as of equal significance with the flushing, each being a vasomotor response. Loss of consciousness was absent in all. The seizures in my cases did not terminate with hiccough, as did those in Penfield's case. Nevertheless the symptomatology in the two cases was justly interpreted as autonomic in nature and correctly attributed to dysfunction of the hypothalamus. That we were dealing with the convulsive state was clear from the paroxysmal nature of the spells and from their association in the same patients with genuine convulsions.

That the interpretation was correct may also be assumed from the fact that ephedrine stopped the lesser seizures; the bromides, which act on the cortex, did not. Conversely, the ephedrine did not in the second case put a stop to those nocturnal attacks, which from their character may be assumed to be cortical in origin. In the first case the major convulsions had no longer occurred and only the petit mal attacks dominated the clinical picture; these the ephedrine promptly stopped.

Without overemphasizing the significance of the two cases, the conclusion is justified that certain types of petit mal attacks are autonomic in nature and that ephedrine seems to have a specific therapeutic effect. The only other observation worth repeating is that accurate isolation and correct interpretation of features which are ordinarily regarded as part of the petit mal attacks may lead to the recognition of a small sub-group and its separation from the larger convulsive state. If this observation is correct it may have some little physiological, anatomical, and pharmacological importance.

² Penfield, Wilder: Diencephalic Autonomic Epilepsy. *Arch. Neurol. & Psychiat.*, 22: 358, 1929.

SPONTANEOUS SUBARACHNOID HEMORRHAGE WITH SIGNS OF A FOCAL LESION IN THE BRAIN*

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Spontaneous subarachnoid hemorrhage is not a rare occurrence in neurological wards and in clinical practice. The usual cause of this type of meningeal hemorrhage is rupture of an intracranial aneurysm. These vascular dilatations may occur in hypertensive disease, in the course of subacute infectious endocarditis with embolisation of the vessel wall, or on the basis of congenital hypoplasia of the arterial tree with disappearance of the elastica (poor tubing of Osler).

The clinical symptoms due to such intracranial hemorrhages consist essentially of meningeal phenomena following an apparent acute vascular episode. In cases that survive the initial rupture, there develops a syndrome consisting of headache, stupor, rigidity of the neck, positive Kernig phenomenon, fever, bradycardia, and even leucocytosis, with either scant or no focal signs. Spinal puncture yields a characteristic non-clotting, sanguineous fluid which, on standing, shows supernatant xanthochromia.

I have encountered four cases which presented, in addition to the signs of subarachnoid bleeding, evidences of a focal lesion of the brain. In two cases aerographic studies were carried out; in the other two this measure was not resorted to. In three of the cases complete recovery has taken place and in the fourth instance the patient has almost fully recovered from a severe left hemiplegia.

CASE REPORTS

Case 1. Anna E., a fifty-six year old widowed housewife, born in Germany, was admitted to the Neurological Service of The Mount Sinai Hospital on September 8, 1930.

Family History. The patient's mother died of locomotor ataxia.

Previous History. Three years prior to admission, the patient fell, head first, and sustained an injury to her skull, but there was no evidence of fracture or concussion. She had been suffering from fatigue and dyspnea on exertion for two years prior to admission. Her menopause occurred at the age of forty-nine.

Present Illness. In May, 1930, the patient was seized with a sudden attack of projectile vomiting and severe headache. She was forced to remain in bed for one week, owing to continuous headache. In June 1930 she had a similar spell. She then remained symptom-free until the onset of the episode which led to her admission

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to the hospital. Her chief complaints on admission were pains in the head and in the spine.

Neural examination revealed right-sided hemiparesis with exaggerated deep reflexes, diminished abdominals, and positive Babinski on the right, meningeal signs, bilateral papilledema, more pronounced on the right, with signs of retinal arteriosclerosis; a certain akinesia of thought and action, slow pulse, divergent strabismus due to weakness of the internal recti, and inequality of the pupils, the left being larger than the right.

Lumbar puncture revealed uniformly xanthochromic fluid which showed the presence of old decomposed blood pigment and was under a pressure of 200 mm. of water.

Serological studies of the blood and spinal fluid proved negative.



FIG. 1 (Case 1). Ventriculogram (anteroposterior view) showing dilatation of the ventricular system.

General medical examination revealed no striking abnormalities. The heart was negative and the blood pressure readings were 130 systolic and 90 diastolic. The pulse rate varied from 64 to 78 per minute.

A flat film of the skull showed no calcification of cerebral vessels.

The diagnosis on admission varied between subarachnoid hemorrhage, due to rupture of an intracranial aneurysm, and frontal lobe neoplasm. Further study showed, in addition to the signs already enumerated, a certain amount of psychic retardation, temporal anomia and perseveration. The patient also was disoriented and exhibited Korsakoff-like symptoms.

Ventriculography was carried out in order to exclude the possibility of an expanding lesion in the left hemisphere. This revealed a symmetrical enlargement of the lateral ventricles and the third ventricle, with some dilatation of the iter, (Figs. 1 and 2) - signs suggestive of a low grade internal hydrocephalus, thus excluding the presence of a supratentorial neoplasm.

After a stay of several weeks in the hospital, the fundus picture cleared up, the mental symptoms improved, although there were some residual defects in memory. The patient was discharged on October 13, 1930.

She was seen in the Follow-up Clinic on December 11, 1930. The patient was alert, cheerful and bright. The hospital period remained a blank in her mind and she "came to" about three days after she left the hospital. She still presented a mild divergent strabismus and slight pallor of the left disc. The pyramidal tract signs had disappeared. The patient had gone back to work and carried out her duties well.

The date of her last visit was November 14, 1935, at which time the patient showed no abnormalities in the neural status and was apparently perfectly well.

Case 2. Moe K., a twenty-one year old auto-mechanic, was admitted to the Neurological Service of The Mount Sinai Hospital on December 22, 1930.

Family History. Negative.

Previous History. The patient suffered from occasional headaches.

Present illness began four days prior to admission with a sudden onset of left-sided weakness and numbness. There was no loss of consciousness but the patient appeared dazed. Two days previously he had suffered from pain over the right eye. On the day of the onset of his illness he also vomited a number of times. The

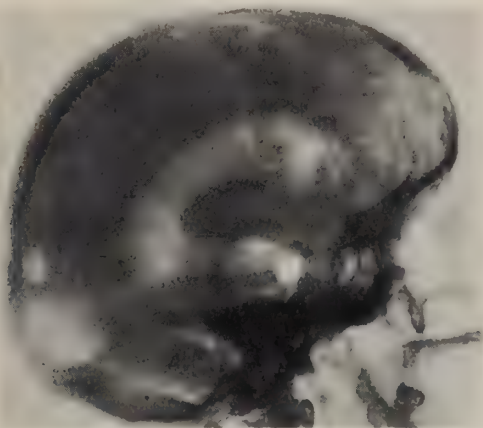


FIG. 2 (Case 1). Ventriculogram (lateral view) showing dilatation of the lateral and third ventricles, aqueduct, and fourth ventricle.

next day there was a slight return of power and feeling. The patient became restless and confused. He rolled from side to side, his attention was poor and he had to be urged to cooperate.

General medical examination revealed no abnormalities. The heart was negative, the blood pressure was 124 systolic and 70 diastolic; the pulse rate 56 per minute. There was a left hemiparesis, both motor and sensory. This was especially pronounced in the upper extremity. There was a slight ptosis of the right upper lid (suggestive of a lesion at the base). The deep reflexes were increased bilaterally but the abdominals were exhaustible on the left, Babinski and Rossolimo signs were elicited on the left. Definite meningeal signs were present. Conjugate movement of the eyes was poorly carried out. The fundi were negative (myopic). The visual fields were normal. The mild right-sided ptosis and the left-sided hemiparesis suggested a lesion in the vicinity of the right crus, a favorite site for aneurysms.

Lumbar puncture yielded uniformly bloody fluid. After sedimentation, the supernatant fluid was definitely xanthochromic. The intrathecal pressure was 160 mm.

Serological studies of the blood and spinal fluid were negative.

The hemiparesis and hemi-sensory changes persisted for a time. The sensory disturbances were those referable to the posterior columns and were accompanied by astereognosis. The patient's symptoms gradually improved and he was discharged on January 21, 1931 with the diagnosis of subarachnoid hemorrhage due to the rupture of an intracranial aneurysm.

He was seen in the Follow-up Clinic. For a time he showed residual left-sided signs, but on May 26, 1932 the patient had no complaints, there were no residual physical signs, and the case was closed.

Case 3. Hattie K., a forty-one year old married housewife, was seen by me on April 23, 1935, at her home.

Family history showed some allergic tendencies.

Previous History. The patient used to suffer from pre-menstrual migraine and for a short period had been showing a tendency to hypertension (160/100). About eight months previously an oculist had told her that there had been a hemorrhage in the left eye. She also suffered from periodic headache and three weeks prior to my visit she had a spell of vomiting and diarrhea, but no urticaria.

Present illness began suddenly one week previously, with a terrific headache, which she described as a "shock in the brain." This was accompanied by a great deal of pain in the back of the neck and was followed by nausea and vomiting. After a few days she developed rigidity of the neck, but no fever. There was no loss of consciousness or stupor.

On April 20 (three days prior to my visit) lumbar puncture was performed. It yielded uniformly bloody fluid which the attending physician thought was traumatic in origin. The pressure reading was 320 mm. of water.

The next day the temperature rose to 102°F. and on the date of my first examination it was 100.6°F. Meningeal signs and left-sided paresis with pyramidal tract signs were elicited. The patient was fairly well oriented, but seemed stuporous and cooperated with difficulty. The right pupil was larger than the left (mild suggestion of a third nerve lesion on the right). Both pupils responded fairly well. The right fundus showed a hyperemic disc with obscuration of its outlines. The left eye was myopic and showed old chorio-retinitis. In addition to the left-sided motor phenomena there was impairment of sensation, especially in the left upper extremity; the sensory disturbances involved position and vibratory sense more than pain and temperature sense and were accompanied by astereognosis in the left hand. The heart revealed a loud aortic second sound and the blood pressure readings were elevated.

A tentative diagnosis of subarachnoid hemorrhage in the course of hypertensive vascular disease was made. A second possibility, namely, cerebral neoplasm with subarachnoid bleeding, was considered; the latter seemed less likely, owing to the acute onset of symptoms and the preceding history of hypertension.

The family physician later reported that the patient was doing well; she had improved considerably and, by June 3, 1935 (six weeks later), had made an uneventful recovery, except for occasional residual headache and stiffness of the neck.

She was re-examined by me on March 6, 1936. There were no neural abnormalities. The blood pressure readings were 150 systolic and 90 diastolic. The patient was attending to her duties as mother and housewife.

Case 4. Sol R., a twenty-three year old bank clerk, was admitted to the Neurological Service of Beth Israel Hospital on January 14, 1936.

Family History. Irrelevant.

Previous History. Occasional attacks of epistaxis.

Present Illness. On January 8, 1936, the patient awoke and blew his nose rather vigorously. He suddenly grew very weak and felt his left arm and leg trembling. A physician who was called administered a sedative to relieve the patient's symptoms. Lumbar puncture revealed the presence of uniformly bloody spinal fluid. When the patient awoke he found that he could not move his entire left side.

Physical examination on admission to the hospital, six days later, revealed a complete left hemiplegia with a pseudoperipheral type of facial palsy and signs of meningeal irritation. The spinal fluid was xanthochromic; the pressure reading was 156 mm. A diagnosis of subarachnoid bleeding due to rupture of an intracranial aneurysm was made and the focal signs were considered part of this syndrome. The fundi were normal. For the next few days the patient showed rapid improvement in the left-sided weakness but severe headache persisted. About two weeks later, January 28, he complained of intense headache and vomited; the pulse became slow and the discs showed early swelling. Lumbar puncture was again performed. The intrathecal pressure was 420 mm. and the fluid was still xanthochromic. The



FIG. 3 (Case 4). Ventriculogram showing a low grade dilatation of the ventricular system.

discs became progressively more edematous. Paralysis of both lateral recti developed and the meningeal signs continued. The intrathecal pressure readings varied from 400 to 460 mm.

Owing to the increasing papilledema, the persistence of left-sided signs, the bilateral external rectus palsy, and the high intrathecal tension, ventriculography was performed (to rule out the presence of an expanding lesion) (Fig. 3). The graph showed slight dilatation of the lateral and third ventricles. There was no shifting of the ventricular system to either side. The ventriculogram was interpreted as having ruled out the presence of a neoplastic lesion. The subsequent therapy consisted of dehydration and daily lumbar punctures.

The objective signs persisted, however. On February 29, while the patient was on the bed-pan, he suddenly lost consciousness and had a generalized convulsion. About two weeks later there were two episodes of left-sided trembling. On March 30 encephalography was performed, in part for diagnostic purposes and in part to forestall the development of possible adhesions at the base (Fig. 4). The graph again showed the presence of a low grade symmetrical internal hydrocephalus and relative

paucity of surface markings. Incidentally, it revealed the patency of the foramina of Luschka and Magendie, indicating that the hydrocephalus was not obstructive in origin, but rather due to blocking of the absorptive channels.

Slowly the hemiparetic signs receded, the swelling of the discs diminished, the intrathecal pressure readings began to fall, and the spinal fluid became clear and colorless. There was a transitory pleocytosis which later disappeared.

Neural examination on October 26, 1936 revealed normal disc outlines, unimpaired visual acuity in both eyes, intact extraocular muscles, slight left facial weakness present only on voluntary innervation, residual weakness in the left thumb and index finger, but no further abnormalities in the neural status.

Summary. Four cases of spontaneous subarachnoid hemorrhage with signs of a focal lesion in the brain have been described. In three of them,

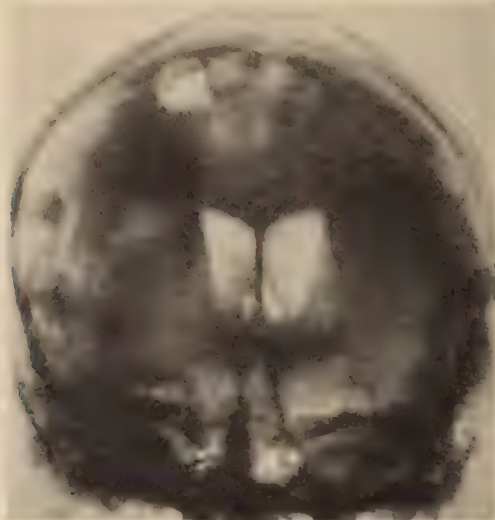


FIG. 4 (Case 4). Encephalogram, carried out six weeks later, showing also a moderate dilatation of the ventricular system.

complete recovery has taken place and in one instance the patient shows only minor residua of the lesion.

DISCUSSION

While the presence of focal signs is occasionally mentioned in the literature, there are very few references to the fact that they played a major rôle in the clinical syndrome. Boudet (1) mentions the occurrence of focal signs in meningeal hemorrhage, and Popow (2) reported two cases with astereognosis as a focal symptom; both recovered. Hemiparesis has been noted on occasion without involvement of the brain substance and has been ascribed to a hematoma over the motor cortex.

The reason for the papilledema, which in some of these cases appears

late in the course of the illness, has been variously given. Occasionally, blood enters the optic sheath and gives rise to a hematoma with pressure on the vessels and resulting papilledema.

Some hold that seepage of blood along the subarachnoid space toward the posterior fossa with occlusion of the foramina of Magendie and Luschka would account for the development of internal hydrocephalus and thus for the incidence of papilledema. I do not believe this is the case. The reason for the papilledema, in my opinion, is the fact that the extravasated blood collects at the site of the perforation and forms a massive fibrin clot at the base of the brain, that this clot later undergoes organization and that the cerebrospinal fluid is thereby prevented from reaching the arachnoid villi where it is normally absorbed, thus giving rise to what Foerster has called a hydrocephalus aresorptorius and what Dandy calls a communicating hydrocephalus. That this is the fact, it seems to me, is proved by the encephalogram in the last case. We were able to fill the ventricles from below, thus eliminating the possibility of block of the foramina of exit from the ventricles.

It is my feeling that the hemiplegia in these cases occurs as a result of seepage of blood into the Sylvian fissure and the interstices of the brain, following the course of the subarachnoid space into the hemisphere. As this blood is absorbed, the hemiplegic phenomena, of course, recede.

That this is the basis for the focal signs, I have been able to convince myself from study of post mortem findings. One must also consider the possibility that the aneurysm may arise from the middle cerebral or Sylvian artery.

I should also like to call attention to the fact that the symptom complex in the last case is very similar to that which Symonds described in his cases of "otitic hydrocephalus." There is the combination of papilledema, bilateral external rectus palsy, and a very high intrathecal pressure (from 400 to 500 millimeters of water). And it seems to me that possibly the explanation for "otitic hydrocephalus" lies also in the fact that there is a disturbance in the absorption mechanism, so that the arachnoidal villi cannot carry off the fluid as rapidly as they do in normal people. That there is no foraminal block in these cases of otitic hydrocephalus has been proved in our work on encephalography.

There was no evidence suggestive of angioma in any of our cases, nor were there signs of a blood dyscrasia.

Although these cases are being cited as purely clinical reports, I feel reasonably certain of the accuracy of our observations.

In conclusion, may I suggest that one might remember this clinical syndrome and give it consideration in the differential diagnosis of neoplasm of the brain. In the latter, the onset is less acute, the predisposing factors are not present, and the subsequent march of events yields more and more

evidence of a focal expanding lesion. In doubtful cases aerographic studies are a helpful diagnostic aid.

I wish to express my indebtedness to Dr. Israel Strauss for permission to report the first two cases from his service at The Mount Sinai Hospital.

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THE VALUE OF MUSCLE TRAINING IN THE TREATMENT OF PARALYSIS AND DISTURBANCES OF MOVEMENT

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The treatment of various forms of paralysis and disorders of coordinated movements in diseases of the central nervous system has long been neglected by most neurologists. It is unfortunately too true that most patients suffering from these conditions who come to the neurologists are considered by them only from the standpoint of diagnosis. Very little thought is given to the possible results that can be obtained by the application of persistent and properly directed muscle training in the treatment of spastic or flaccid paralysis and in the various disorders of movement as seen in tabes, tic and chorea. Such patients are often left to their own devices in coping with their disabilities or are at best relegated to the care of lay persons, masseurs or physiotherapists, most of whom have no conception of the physiological and psychological problems that may be involved, and which must be considered in each individual case for the successful outcome of its treatment.

It has long been recognized that there is a psychological as well as a physiological element in most symptoms, especially those associated with a disability resulting in such partial or complete immobilization as occurs in hemiplegia, poliomyelitis and tabes dorsalis. Maloney, in his book "Locomotor Ataxia," emphasizes the importance of recognizing and treating adequately the psychological elements that occur in the manifestations of organic diseases of the nervous system. The mental state in these patients indeed becomes an important factor in the care of and ultimate outcome of their disability.

To meet the requirements of life with such a disability as exists in tabes and in hemiplegia requires strenuous efforts on the part of the individual thus affected; minimal results are obtained with maximal efforts. This not only results in extreme fatigue but undoubtedly tends to intensify the already existing disturbed mental state of the patient resulting from the threat to his ability to get about. Fear complexes readily form, and as they become elaborated, they tend to succeed one another and produce an unrelieved state of doubt and mental perturbation. Frequently, irritability and depression add to the patient's misery, and demoralization becomes more complete as unenlightened treatment fails to improve his existing physical condition. With the use of the breathing and relaxation exercises, which will be described later, and of mechanical measures such

as corrective shoes, braces, splints and casts, these mental states can be successfully combated and largely avoided.

Too little, if any, attention by the neurologist or the internist is given to the prevention of contractures and periarthritic changes, that are sure to occur, in conditions such as hemiplegia and poliomyelitis where reciprocal muscle action is disturbed. The immediate application of a simple splint to maintain the paralyzed part in a physiological position, and the use of passive movements at the immobilized joints, will go far to reduce or to obviate these distressing and disabling complications of hemiplegia. For use in hemiplegia, I have devised a brace made of aluminum which extends from the middle of the arm to the finger tips. The metal is sufficiently pliable to allow molding at the fingers and wrist so that gradually increasing extension of the wrist and fingers can be obtained. The brace or splint should be used both during the day and night except when the exercises are being given and should be removed only if it becomes very annoying. The casts in poliomyelitis should be split and removable so that exercises and other physical measures may be administered without interruption. In tabes, the more an ataxic patient walks uncorrected the more ataxic he tends to become. It is difficult to cure a symptom which is constantly being aggravated. Mechanical measures were devised and suggested by Maloney for the immediate reduction of ataxia. These measures are used only as temporary aids, and are discarded as soon as the ataxic regains control of his movements, and the muscles are sufficiently developed to carry on their normal functions. When standing or walking the average ataxic tabetic rotates his feet outward and in a horizontal plane around a vertical axis, which passes through the ankle joint, to such an extent that the distance between the great toes may be several times that which separates the heels. These abducted feet are usually overpronated and in some cases, on account of the hypotonis and constant overstretching of the ligaments, the anteroposterior and the transverse arches yield. Such a foot affords a poor and inadequate support; the only stable element in it may be the *os calcis*. The lack of support that such deformed feet afford to the swaying tabetic creates in him at every step not merely uncertainty, but even a lively fear. The instability and fear result in excessive expenditure of muscular and nervous energy and contribute largely to fatigue. For the correction of this condition Maloney has devised a plate for the arches. This plate is constructed from models of casts of the foot taken when at rest and when the foot is bearing the body weight. The plate is a modification of the Whitman plate. The inner lip is curved below the level of the scaphoid; the outer flange is lower and does not extend as far forward; the support of the transverse arch extends outward beneath the four inner toes. When the spread is very great, the inner lip is extended forward to include and completely surround, on the inner side, the first metatarsophalangeal joint. The plate is further reinforced by using a

high shoe. The last of this shoe is straight and an extension of the sole three-eighths of an inch is recommended. A hickory-wood filler extends from the heel, through the shank, to the front of the sole, rendering the sole rigid and unbending. The heel is wedge-shaped with the base of the wedge on the ground; it is seven-eighths of an inch high and is partly of cork to insure lightness. The box of the shoe is high; the tongue is thick and soft so that the shoe can be laced tightly; the ankle is reinforced with a small leather brace inserted between the lining and the upper. The special features of the shoe are its rigidity, its lightness, the increased ground area of the broadened sole and heel, and lastly the support around the ankle which prevents the ankle from yielding.

The importance of the proper use of orthopedic appliances in the treatment of paralysis following poliomyelitis is familiar to all and scarcely needs to be emphasized. However, it is well to remember that there are few indications for early surgical intervention in poliomyelitis, and in the absence of these (flail joints, progressive scoliosis, etc.) persistent muscle training and development in addition to the other physical measures should be continued for at least two years, and even longer in some cases, before corrective operative procedures are attempted. The greater the development that can be obtained in the muscles used for transplantation, the more satisfactory are the results to be expected from the surgical procedure. Muscles apparently totally paralyzed have been noted, with persistent training, to regain their function after periods of one, two, and even more years of complete inactivity. In poliomyelitis there is no single guide to indicate when and to what extent a muscle will recover its function. Electrical studies have been of little value, in my experience, but it may be generally said that when the muscle begins to respond to faradic stimulation, the degree of return of function in that muscle will be found to be in proportion to the intensity of its response to the current. I have also noted that the volume of a muscle and its tone will improve long before function is evident. The importance of performing the exercises in a water bath cannot be overemphasized. In water, maximal results of muscle function can be obtained with minimal efforts, and the water bath should be used as a routine part of the treatment in poliomyelitis.

With the groundwork laid by the use of these mechanical measures one can usually proceed with the next step in the treatment, namely, muscle training. The method of reeducation, that has been most successful in my hands, I have adapted from the method advocated by Dr. William J. M. A. Maloney (1), for the cure of ataxia. The exercises may be divided into three stages: 1) breathing; 2) relaxation; 3) muscle training.

The following technic is used to begin the treatment in most cases. Additional exercises for precision in chorea, and to increase the ability to concentrate in overcoming tic movements, will be described later. The rest exercises, consisting of breathing and muscular relaxation, initiate

each treatment. A quiet room, preferably darkened, with a bed or a couch wide enough to keep the patient's arms from hanging over the sides, when relaxed, a small cushion for the head, and a metronome to regulate the time are the only appliances required. The patient in a recumbent position, with clothes about the chest and abdomen loosened, is instructed to breath deeply and to pause at the end of both inspiration and expiration. After a few deep respirations have been taken, the patient passes to breathing of moderate amplitude, and later to gentle breathing. The breathing is of the abdominal type, slow in rate, and uniform in rhythm. Thoracic movements are restricted. Distracting thoughts are stopped as they arise, and the patient's attentions must be fixed on the sensations that accompany breathing. A bag of shot or sand placed on the abdomen, increases muscular effort so that the breathing may not readily lapse into an unconscious act. When the breathing has become slow and regular, muscular relaxation is attempted. To relax the muscles passive movements at each joint are used. The muscles of the scalp, forehead, eyelids, and jaw are passively moved until wrinkling of the forehead, and blinking of the eyelids diminish and disappear, and muscular spasm has been reduced or eliminated.

Next a shoulder is relaxed, then an arm, each in turn being passively moved until muscular spasm has been eliminated and the part lies flaccid and motionless or falls limply from any unsupported position. When a part has been relaxed, those parts previously and newly relaxed should be briefly dealt with again in the order in which they were first relaxed. This linking of parts previously to parts newly relaxed is helpful in bringing the whole to a satisfactory state of relaxation. Relaxation of the neck and trunk muscles is best accomplished while the patient sits. The patient's arms should then hang limply at his sides, and his feet, crossed one over the other, should rest on their outer borders. The head should next be passively moved in all directions slowly, and the movement repeated until the head falls limply forward or backward by its own weight. The trunk should be slowly bent backward and forward and from side to side until the muscles are relaxed sufficiently to allow the trunk, unsupported, to gravitate without restraint in whatever direction it is inclined.

Throughout the passive movements, the operator periodically corrects the breathing, slows it as it quickens, insures adequate pauses at the end of both inspiration and expiration. The objective guide to success is the behavior of the eyelids.

When the patient is well relaxed, the eyelids are still, the pulse rate has slowed and the blood pressure has fallen. When the quivering of the eyelids returns, the patient is uncomfortable or distracted. The training usually begins with several ten minute periods separated by short intervals. The quicker the patient learns the less is the strain upon him and the more pronounced is the relief of his muscular, vascular, and mental tension.

These exercises are of greatest value in the treatment of spastic hemiplegia where muscular tension is increased and vascular tension is usually high. It also quickly overcomes fatigue.

The patient is now ready for muscle training. As no movement is permissible except in a correct, well balanced posture, and as the recumbent may be the only perfect posture, the movement exercises are usually begun in the recumbent position. The simplest movements are the easiest to perfect and these should therefore be the ones taught first. The perfection of a simple movement depends upon the perfection of its cardinal qualities, strength, direction, extent and rhythm.

The beginning and the end of a movement should be definitely fixed. For direction and extent of movement, it is first performed passively by the physician; then the patient resists this passive movement. Next the patient attempts to perform the movement guided by the operator, guidance being gradually diminished as the movement becomes more accurate. Finally, the movement is repeated against resistance. These resistance movements are of value in developing power because they can be intensified as the muscles become stronger. For rhythm and rate a metronome can be used.

When the simple movements have been perfected at all of the joints, more complicated movements are attempted involving movement of several joints at the same time. Then combinations of leg and arm exercises are taught, and to these head movements are added later. When the patient is able to perform all of the exercises well in the recumbent position, similar exercises are given at first in the sitting, and later, after he is able to balance well, in the upright position. Finally, he repeats the exercises while moving backward, forward, and from side to side. Each step must be thoroughly mastered before any advance in the exercises is attempted. Attention to detail is necessary and all movements should be learned accurately and be done in rhythm either to counting or to the beat of a metronome. Fatigue must be religiously avoided and as soon as the patient falters in his work the exercises should be terminated for that period. By allowing suitable rest periods between each exercise it is possible to continue working without evidence of fatigue for periods varying between forty-five and sixty minutes. The exercises may be repeated two or three times a day. One of these periods should be done under the supervision of the physician.

In addition to these exercises I have been greatly aided in the treatment of chorea and tic by the use of Brissaud's method (2), and with Oppenheim's method of treating tic (3); Oppenheim calls them "inhibition exercises." These consisted essentially of some form of peripheral stimulation, for example, pinching, pricking, or tickling of the skin; or bringing a sharp instrument toward the patient, with the command to control and repress the desire to move or touch the parts thus disturbed. Brissaud's method

of treating tic is a combination of immobilization of movements, with movements of immobilization. The immobilization of parts involved by the habit movements may be done with the patient sitting or standing before a mirror. The length of time that the patient remains immobile should be gradually increased until he is able to control the tic movements absolutely for five minutes. Then the position of the head, body and extremities may be varied, directing especial attention to performing special exercises in the tic area. At first only simple movements should be attempted, followed later by more complicated ones.

In chorea, if fever is present during the acute stage, only breathing and relaxation exercises should be attempted, for short periods only. Active exercises during the febrile period may even be harmful. Active movements should be begun only after the temperature, pulse, and respirations have been normal for several days, and after the breathing and relaxation exercises have been thoroughly mastered. For precision of movement various games and toys are used. For control of the hands, simple finger exercises, writing, drawing, and painting are of value. The patient should not attempt to stand or walk until all movements are performed perfectly in the recumbent position. Guthrie has systematized a series of exercises, somewhat similar to those outlined above, with which he has had equally good results in the treatment of chorea.

CASE REPORTS

The following cases of poliomyelitis, hemiplegia, tabes dorsalis, chorea and tic will illustrate some of the results which can be obtained with persistent muscle training supplemented by the various measures outlined previously.

Case 1. C. G. was a 21 year old student whose present illness began in September of 1932. The onset was sudden with headache, pain in the back of the neck and fever. The next day the pain had extended to the shoulders and lumbar region of the spine, and she complained of dizziness, nausea, and vomited several times. The following day she again vomited, her temperature rose from 101 to 105 degrees F., and she complained of stiffness of her neck.

Neurological examination on that day revealed a coarse nystagmus in the vertical and both horizontal planes and a facial weakness of the peripheral type on the right side. Fundi and other cranial nerves were normal. There was no definite weakness in the upper or the lower extremities but there was a coarse jerky tremor of both hands and an ataxia in both arms in the finger-to-nose test. The deep reflexes were present and equally active in both arms. The abdominal reflexes were present and equally active. The right knee jerk was absent and the left was diminished. Both ankle jerks were present and normally active. A positive Babinski was present on the right and an equivocal plantar response was obtained on the left side. There were no sensory disturbances. There was moderate rigidity of the neck and a bilateral Kernig sign was present. Lumbar puncture yielded a clear fluid under moderate pressure and showed 156 lymphocytes.

That night she developed a complete flaccid paralysis of all four extremities with

loss of all of the superficial and deep reflexes. Her back, shoulder, intercostal and abdominal muscles were markedly involved. Her abdomen was distended and her breathing was labored. She was sweating and looked anxious.

The irritative stage lasted about four weeks. During this time the extremities were kept in a physiological position with sand bags. As soon as the irritative stage was over passive movements were begun. These were soon augmented with active movements in the muscles that showed indications of return of power. Each muscle group was given a little attention every day. It was soon evident that some of the muscles would regain their power more rapidly than others and on these we concentrated our efforts until definite function was reestablished. The muscles of the left shoulder, arm and leg, with the exception of the triceps, and the flexors and extensors of the fingers, recovered first. The back and shoulder muscles were next developed to the point where the patient was able to maintain a sitting posture with support. In four months she was able to sit out of bed for short periods. Standing with support was next attempted, and walking with support soon followed. Swimming was attempted the following summer and the patient, who was an excellent swimmer before her illness, soon began to move about fairly well. Improvement on the right side was slow. Function returned slowly in the right deltoid, biceps, and triceps, after one and one-half years of apparent absence. She is now able to walk, swim, dance, and attend college, handicapped only by the weakness in her hand muscles. Corrective surgical procedures done last summer showed that all of the muscles of the flexor group of the forearm were viable.

Case 2. F. B., a 12 year old school girl, referred by Dr. H. Kazmann, became ill on August 14, 1934. She complained of stiffness of the neck, pain in the abdomen, headache and fever. Three days later the left leg became paralyzed.

Neurologically she showed a flaccid paralysis of the left leg with loss of the deep reflexes on that side. The anterior tibial and peroneal groups were completely involved while the thigh and other leg muscles were only partly affected. The deep reflexes in the left arm were less active than in the right and there was some weakness in the left biceps, triceps, and in the abdominal muscles on the left side.

With systematic exercises there has been complete recovery in the muscles of the arm, abdomen, and thigh. The peroneal and tibial muscles have shown a marked improvement and are gradually returning to normal power.

Case 3. R. R., a six and one-half year old school boy, referred by Dr. H. Kazmann, became ill in July, 1933. He returned from school complaining of tiredness. The next day he complained of headache, pain in the back of his neck, abdomen and legs. His temperature was 101 degrees F. He became nauseated but did not vomit. He was unable to move his bowels for the next four days. His mother noticed that he could not cough properly and that he was unable to raise himself from a recumbent to a sitting position. He also complained of a peculiar, crawling sensation, under the skin of his right leg.

Neurological examination showed that his pupils, fundi, and cranial nerves were normal. The upper extremities were normal. The abdomen was distended and there was marked weakness in the abdominal muscles. The abdominal reflexes were absent. There was marked weakness in all of the muscles of the right thigh and leg. The right knee and ankle jerks were diminished. There were no objective sensory disturbances. The neck was moderately rigid and a bilateral Kernig sign was present. The spinal fluid was clear, under moderate pressure, and showed 230 lymphocytes.

After the irritative stage exercises were begun, an abdominal belt was fitted and

was used until the abdominal muscles recovered. The muscle power in the right leg returned to normal within two years.

Case 4. H. K., a 64 year old retired merchant, was referred by Dr. M. Rothchild on June 5, 1933. About two weeks previously the patient awoke one morning and found that he was unable to move his left arm and leg; they felt numb and heavy.

A neurological examination showed a complete flaccid type of paralysis on the left side. The deep reflexes were more active on the left than on the right side and a positive Babinski response was obtained on that side. His pupils were normal. His fundi showed moderate sclerotic changes. There was a left central facial weakness. His other cranial nerves were normal. He had a marked, coarse tremor of the right hand.

Muscle training was immediately begun and after about three months he was able to use his arm well and was able to get about without any difficulty.

Case 5. J. J. Q., a 63 year old retired broker, was referred by Dr. C. Prout for treatment. He became faint while in a dentist's chair nine weeks previously. He was able to return to his home but his wife noticed that evening that the left side of his face seemed drawn upward. He then developed a gradually increasing weakness in the right arm and leg. He also had some difficulty in his speech. For several years previously he had known that he had hypertension.

His neurological examination showed a spastic hemiplegia on the right side with the usual signs of pyramidal tract involvement. A slight motor aphasia was still present. There was a marked edema of his right hand. His blood pressure was 220 systolic and 120 diastolic.

Exercises were given for the next three months and he made a fairly complete recovery from his hemiplegia. His systolic blood pressure receded and had remained between 160 and 180 during the last month.

Case 6. A. A., a 47 year old man, was referred by Dr. I. Strauss. His past history showed that he had suffered from malaria eighteen years ago and that he had had a primary lesion thirty years ago. His present illness began about eighteen years ago; after a severe attack of malaria, he began to have sharp shooting pains in his legs. Soon after he began to have similar pains in both arms. For several years he noticed that his memory was failing. He also noticed that his gait became difficult, especially when walking in the dark. His gait gradually became worse until he became so fearful that he used a wheel chair by preference, and stood or walked only when assisted by some person, or with the aid of a cane.

His neurological examination showed unequal, irregular pupils that were fixed to light. He had a marked Romberg, and a markedly ataxic gait. There was a generalized atrophy and a moderate hypotonia of all of the muscles in the upper and the lower extremities. The knee and ankle jerks were absent. Sensory examination showed patchy areas of hypalgesia on both legs, loss of vibration below the crests of the ileum, diminished deep pain sensibility and loss of postural sense below the knees.

Exercises were given for about three months, after which the patient was able to walk unassisted and without fatigue for a distance of two miles.

Case 7. G. B., a 46 year old man, was referred by Dr. I. Strauss. His past history showed a primary lesion twenty years ago; the Wassermann test was said to be negative since treatment at that time. His present illness began about six months ago, when, after the shock following the death of his father, he began to have difficulty in

walking. This was especially noticeable when he entered a dark room or closed his eyes when standing. At about the same time he noticed a tremor of his right hand. Since that time his gait had become progressively worse so that he had to use a cane to get about.

Neurological examination showed slightly unequal, irregular pupils that reacted to light and on convergence. His fundi and other cranial nerves were normal. He walked on a broad base and showed a moderate ataxia in his movements. There was a marked Romberg present. He showed a coarse tremor of both hands. The deep reflexes were diminished in both arms, and the knee and ankle jerks were absent. Moderate hypotonia was present in the muscles of both legs. Sensory examination showed loss of vibration below the crest of the ileum, and disturbance of postural sense in the toes of both feet. He was cured of his ataxia after ten weeks of treatment.

Case 8. S. H., an 8 year old school girl, was referred by Dr. I. Strauss. Her family and past histories were negative. At the age of six she had an acute attack of chorea which became progressively worse despite treatment. It had lasted many months before she came under my observation. On examination she showed intense choreiform movements of all of her extremities. Her face was continuously distorted by grimacing. Her respirations were irregular and speech was almost impossible. She was moody, irritable, and very unstable emotionally. She was suspicious and difficult to approach. Later she became more cooperative and tried to help with the exercises. I saw her at irregular intervals and showed the nurse and the mother how to proceed with the exercises. Soon she began to improve and after about ten weeks she made a good recovery. The exercises, which should have been continued for some time after she recovered were discontinued by the mother. The following summer the patient again began to have choreiform movements. These were controlled by again using the exercises for a few weeks. Since that time she has remained perfectly well.

Case 9. E. L., a 9 year old girl, was referred by Dr. I. Strauss. Her past history showed that she had had measles and chicken-pox two years ago. Her mother stated that since that time she had had several mild attacks of choreiform movements. About six weeks previously the patient began to have difficulty in her speech and in walking. She also began to have irregular movements of both arms. Since then she had become progressively worse.

Neurological examination showed moderately severe choreiform movements of the face and all of her extremities. Her speech was somewhat involved. I saw her at irregular intervals and showed the mother how to direct the exercises. She made a good recovery in about six weeks and remained well until April of 1933. At this time her mother noticed that she became restless and that occasionally mild twitching of the muscles of the arm was present. The exercises were employed two weeks after the onset of this attack and she made a prompt and complete recovery.

Case 10. H. R., 15 years of age, was referred by Dr. E. Bick. The past history was negative except for the usual diseases of childhood. At about the age of four years the mother stated that the patient began to have a blinking tic of both eyelids. This soon extended to the muscles of the face causing facial grimacing. At the age of twelve years he began to have movements affecting the right shoulder and the right arm. With great effort he could at times suppress these movements for short periods.

Neurological examination showed a typical clonic blinking tic of the eyelids,

moderately severe facial grimaces, and a shrugging tic of the right arm. Exercises were begun and within eight weeks the tic movements disappeared. His mother states that he blinks his eyelids only when he becomes exceptionally excited but he is able to control these movements as soon as his attention is called to them.

Case 11. T. J., seventeen years of age, was referred by Dr. W. Sheldon. His past history had no bearing on his present illness. At the age of ten years the patient began to have a tossing movement of his head. At times he was able to control this, but twitching of the facial muscles occurred instead. He stated that he had an irresistible desire to perform the movement resulting in a feeling of satisfaction when it was accomplished. His neurological examination showed nothing of significance except a tossing tic of the head. Exercises were given over a period of seven weeks and the patient was discharged cured of his tic.

SUMMARY

It may be pointed out that with the simple methods outlined above much can be done to help patients suffering from the various neuromuscular disorders characterized by paralysis and loss of control of movements.

The psychological element in the clinical picture of each case is as important as the physiological element and must not be neglected in the care of these patients. The extent to which a patient is influenced by this psychological factor is usually indicated by the variations of the clinical well-being of the patient and by his mental state.

Fatigue, so readily induced in these patients by the added effort necessary to overcome the handicap due to their disability, must be reduced to a minimum before efficient function of the disabled parts can be expected. The "rest exercises," previously described, help to reduce internal distraction with its resultant mental stress; they obviate the unconscious muscular spasm and contractions that are so commonly present in these patients, and promptly control the fatigue which results from these states. Finally, it must be emphasized that the greatest care and patience with one's self are necessary. The patient should never be asked to perform any exercises for which he has not been properly prepared. Perfection of all the simple exercises preceding the complicated ones should be insisted upon before he attempts the complicated one, as failure tends to demoralize him and undermines his confidence in the treatment.

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CARDIAC ARRHYTHMIAS WITH SPECIAL REFERENCE TO PAROXYSMAL TACHYCARDIA, AURICULAR FIBRILLATION AND PREMATURE BEATS IN CONSTITUTIONALLY ALLERGIC INDIVIDUALS*

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"Recurrent palpitation of extreme rapidity in persons otherwise apparently healthy," was first described by Bristowe in 1888. The following year Bouveret designated this syndrome as "paroxysmal tachycardia." Its close relation to premature beats was clearly recognized. With the increased knowledge of cardiac arrhythmias obtained by the electrocardiogram a more precise differentiation of tachycardia into auricular and ventricular, was made possible. This distinction when correlated with the clinical course and the pathologic findings has led to the realization of the more serious prognosis in ventricular as compared with auricular tachycardia. The latter with its inconstant pathologic substrate, its sudden onset and termination, represents a reversible reaction of varied etiology usually occurring in a heart otherwise healthy. Paroxysmal auricular fibrillation may be seen in normal healthy individuals.

The exciting agents of paroxysmal tachycardia have been attributed to fatigue, sudden exertion, indigestion, tobacco, alcohol, digitalis poisoning, infections and reflex vagus stimulation. Those of paroxysmal auricular fibrillation have also been assigned to "toxic influences." The underlying causes are frequently obscure in both.

Since most of the predisposing factors above enumerated, with the exception of infections or digitalis, represent the daily contacts of the average men in whom no such dramatic cardiac arrhythmias supervene, the question naturally arises whether there is not in addition to the external agent some constitutional factor responsible for the precipitation of such paroxysms. Individual hypersusceptibility, i.e., allergy to various excitants, with the heart as a shock organ,¹ similar to the condition existing in asthma where the lung is the shock organ, may be a plausible explanation.

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Subsequent to the presentation of this report a paper dealing with the subject of Food Allergy with special reference to Paroxysmal Tachycardia and Essential Hypertension appeared by L. F. Gay in the Journal of Missouri State Medical Association, 332-338, September 1937.

¹ "Shock organ" is used in a general sense to indicate the seat of reaction.

The approach from the point of view of allergy, however, is beset by the many difficulties common to this field because laboratory support in the form of experimental or post mortem evidence is not always available. The proof of an allergic mechanism must therefore be obtained by essentially clinical methods such as skin tests: elicitation of symptoms on contact with the reacting allergen and their cessation on withdrawal. That such means are successfully utilized in the diagnosis and treatment of the accepted allergic diseases such as asthma, hay fever etc. is generally recognized. The person presenting any of these manifestations is regarded as definitely allergic and the organ reflecting this mechanism is considered the shock organ. That tissues other than those in the respiratory and gastro-intestinal tracts or skin, may become shock organs, as for example the heart and blood vessels, has not been generally acknowledged. The acceptance of the cardiovascular system as a shock tissue in the allergic sense, is made difficult not only by lack of sufficient pathological and experimental criteria, but also by the reluctance on the part of some clinicians to accept as evidence positive skin reactions where the sole presenting symptoms are referable to the heart or blood vessels. Indeed some allergists assign special atopic attributes to asthma, hay fever, certain forms of skin or gastro-intestinal hypersensitiveness, to the exclusion of all other organs. Inasmuch as the constitutionally allergic patient is an integrated unit, it is logical to suppose that in such an individual any tissue or system may be the seat of allergic reactions.

To prove that certain symptoms provoked by a less familiar shock organ can also be due to hypersensitiveness, it is best to select at first only such cases which fit into the allergic framework on the basis of an inherited allergic constitution. Such cases must therefore satisfy the following criteria: a) family history of allergy; b) the presence of well known allergic manifestations; c) eosinophilia; d) positive skin reactions to antigens capable of eliciting the presenting symptoms and e) a cessation of these symptoms on withdrawal of the offending allergens.

The following cases, observed from one to ten years with symptoms referable to the heart as the major shock organ, fulfill most of these postulates. The cardiac manifestations alternated or were associated with allergic symptoms in minor shock organs, such as the skin, gastro-intestinal and respiratory tracts. Two of our patients had paroxysmal tachycardia and premature beats, brought about by specific protein hypersensitiveness; one had auricular fibrillation and angina pectoris.

CASE REPORT

Case 1. History. B. A. S. age 26, was first seen in October 1935 referred by Dr. C. Miller with the diagnosis of paroxysmal tachycardia. The patient's grandfather, mother and brother had asthma, and one cousin had hay fever. The patient had had scarlet fever, pneumonia, diphtheria and measles. Throughout the year

he was subject to frequent head colds, vasomotor rhinitis and pharyngitis. Since January 1935 he had been having attacks of discomfort about the chest especially in the precordial area. These symptoms were characterized by attacks of palpitation and would occur especially at night before, or soon after, he got into bed. One severe attack of palpitation, however, occurred in March 1935, while he was on a train sitting comfortably in a Pullman chair. During one of his attacks he was examined by Dr. Poll. The heart rate was 172. Compression of the carotid sinus slowed the rate for several minutes, but releasing of the pressure was followed by a return of the tachycardia. In view of the absence of organic physical abnormalities Dr. Poll prescribed gynergen and luminal. The medication apparently controlled the attacks for about two months, but after that they recurred. This time, however, the cardiac palpitation was first preceded by abdominal pain in place of his former chest pains. His physician attributed this condition to a spastic colon, and advised him to take atropin and sodium amytal. Although the abdominal discomfort was allayed for a time under this regime, the attacks soon returned again, especially on going to bed. The patient claimed that the abdominal pains would begin in the pit of his stomach, radiate to his legs and testicles, and after about an hour would be succeeded by an attack of palpitation of the heart.

Examination. The patient was a well nourished and a very apprehensive, but otherwise healthy, young man. The eyes, ears and nose were negative. The heart outlines were normal and no adventitious sounds were heard. Muscular quality was good. The pulse rate was 78 per minute. The blood pressure was 120 systolic and 60 diastolic. The abdomen and extremities were negative. The skin was normal.

In view of the family history of allergy, the frequent head colds, irrespective of the season of the year, as well as gastro-intestinal disturbances, preceding the cardiac symptoms, it was deemed justifiable to investigate whether a common mechanism, that of protein hypersensitiveness, was responsible for these varied manifestations.

Study from the allergic point of view by means of intradermal skin tests, showed him to be sensitive to the following: wheat, oat, rice, lamb, clam, oyster, crab, flounder, shrimp, asparagus, brussel sprouts, cabbage, cauliflower, corn, cucumber, lettuce, lima beans, peas, mushroom, onion, tomato, squash, string bean, orange, apple, peach, cantaloupe, cherry, chocolate, cashew and filbert nuts.

He was placed on a diet omitting these foods and for the first time in several years felt well. In his own words "I can work sixteen to eighteen hours a day, without fatigue." His appetite was good and he had lost his sense of apprehension. With the object of increasing his diet we began in November 11, 1935 to experiment with some of the foods to which he reacted, in order to isolate if possible the ones responsible for his symptoms. He ate asparagus and lettuce at dinner. Three hours later, he felt distended and experienced precordial distress with a paroxysm of sudden and rapid pounding of the heart, which lasted for about a half an hour. After this ceased he was completely exhausted and fell asleep. The next day he complained of a sore throat, general malaise, rapid pulse, and palpitation. Examination disclosed a reddened throat and edematous adenoid follicles in the nasopharynx. His temperature was normal. These findings were interpreted as being due to food hypersensitiveness and not to infection. The heart was rapid and irregular, with five to ten extrasystoles per minute. The rate was 160. Abdominal examination was negative. He was advised to take Epsom salts. The next day his palpitation was gone. The pulse had become slower, but he still had occasional extrasystoles, and was somewhat hoarse. Two days later he was completely well.

He was not seen again until December 24, 1935. He stated that on December 20 he had a vegetable lunch, consisting of cabbage, lettuce, tomatoes and whole wheat

bread. Immediately after he had finished this combination of foods, he experienced palpitation. He was not especially distressed except that the extrasystoles continued for three days until December 23. That evening he had some lamb chops. (He had given positive skin reactions to lamb.) The extrasystoles continued until the following morning when he began suddenly to experience a sense of abdominal distress, which traveled upward to his chest and culminated in a severe attack of palpitation. The paroxysm was so violent that he was forced to lie down. The attack continued at its maximum tempo for about two hours. Examination an hour later disclosed a heart rate of 130 to 140. Electrocardiogram taken by Dr. S. Averback two hours later showed a sinus arrhythmia, and auricular premature beats. The PR interval was 0.20 seconds. The T-waves were upright. No preponderance was present. The heart rate was 110. He was given an enema and colonic irrigation, and the attack promptly subsided, except for occasional premature beats throughout the day.

After this experience he stayed on his diet until January 6, 1936, and felt perfectly well. That day he ate some lamb, lettuce and tomatoes and three hours later developed an attack of palpitation and extrasystoles. He took some cascara, moved his bowels and the next day felt well. On January 11, 1936, he ate lamb, cabbage and peas. This was followed by running of the nose, itching of the eyes and severe attack of palpitation, which lasted for two days. Treatment consisted of catharsis. On January 19 he ate lettuce and tomatoes, but had no cardiac symptoms. Several days later he ate cauliflower and lamb. This combination of foods was promptly followed by an attack of palpitation. Catharsis caused a disappearance of the symptoms.

We then decided to omit the lamb, cabbage and cauliflower (temporarily), which had given rise to symptoms, and added other positively reacting foods to his diet with the following results. Chocolate made him uncomfortable and he experienced abdominal cramps, but nothing else. Potatoes, spinach, cheese and coffee were well tolerated. After a heavy meal of the permitted foods plus the ones which were found to give positive skin reactions he would feel distended, but he had no increased heart rate nor extrasystoles. On February 24, 1936, he ate lamb and cabbage for lunch. This was followed three hours later by distension and palpitation which lasted fifteen to thirty minutes. On February 26, 1936, he again ate lamb and cabbage. This was again followed two hours later by palpitation which lasted one hour. On February 28, 1936, he ate cauliflower only, but with no after effects. The next day he again ate cauliflower. This was apparently beyond the threshold of his tolerance and was followed by palpitation about one hour later, which was of short duration. On March 2, 1936 he partook of lamb and cauliflower. This was followed by coryza, sweating, coughing, and three hours later, palpitation. His temperature was 100 F. On March 5, 1936 he had lamb and cauliflower for lunch with similar results, i. e., two hours later coryza, cough and sweating. In the evening he developed an attack of palpitation lasting two hours.

Following these experiences he omitted the offending foods from his diet and felt completely well, until March 30, 1936. That day, three hours after eating shrimp to which he was sensitive, he developed a paroxysm of palpitation which lasted one hour followed by extrasystoles, which continued for sixteen hours. In June 1936, he was asked to eat lamb again. After eating lamb for two days in succession a brief attack occurred, which lasted only one half hour. Following this attack he developed a sore throat, a coated tongue and clogging of nasal passages, due to swelling of his turbinates.

Complete removal of the above mentioned foods from his diet has been followed by freedom of cardiac, respiratory as well as abdominal symptoms.

This patient has been seen in 1938 and has been free of symptoms.

Summary, Case 1. A young man of 26 with a family history of asthma, who had been subject to frequent attacks of vasomotor rhinitis, developed cardiac symptoms of palpitation for the past two years. Study from an allergic point of view by skin tests indicated that he was sensitive to various foods. Their clinical significance was verified by ingestion. It was found that lamb alone, or lamb in combination with cauliflower, cabbage or lettuce, tomatoes and peas, invariably induced a rapid heart rate with premature beats lasting from several hours to one or two days. The heart rate during the attacks varied from 110 to 172. On at least one occasion there was a definite attack of paroxysmal tachycardia. Lettuce and tomatoes alone were tolerated without any ill effects. Lettuce and tomatoes in combination with whole wheat bread produced extrasystoles but no acceleration of the heart. Lettuce and asparagus were followed by rapid heart rate. Cauliflower alone within certain limits was without effects. Larger quantities of cauliflower were succeeded by moderate increase in pulse rate. Removal of lamb, cabbage, asparagus and cauliflower from his diet was followed by freedom from cardiac and upper respiratory symptoms.

That the mechanical factor of abdominal distension alone was not responsible for his paroxysms was demonstrated by the eating of a large meal, consisting of tomatoes and lettuce etc., which caused distension and discomfort, but did not produce cardiac symptoms. Certain specific foods such as lamb, cabbage, cauliflower, asparagus and wheat alone or in combination produced definite cardiac symptoms.

Case 2. History. The patient E. Y., aged 37, was referred by Dr. Reuben Ottenberg, because of recurring paroxysmal tachycardia. When seen by him on November 28, 1925 she complained that for four weeks she had had bouts of cardiac palpitation which lasted a few minutes at a time. Her past history threw no light on this symptom. She had had a tonsillectomy and a submucous resection in 1913, because of frequent nasal colds with obstruction. She was subject to mild attacks of indigestion, and had an attack of jaundice at the age of 13. She was moderately constipated.

Examination disclosed a rather tall individual, 5 feet 10½ inches. The features were somewhat acromegalic. The eyes and ears were negative. There was some obstruction in the nasal passage. The lungs were normal. The heart was not enlarged. There was no evidence of valvular disease. The blood pressure was 112 systolic and 80 diastolic. The heart rate was between 116 and 128. She had four extrasystoles to the minute.

Electrocardiographic examination by Dr. Herman Mond during the attack showed a "paroxysmal tachycardia of auricular origin and a rate of 210. The ventricular complexes were normal except for an inversion of the T-waves in lead 3. The auricular complexes were hidden in T-waves."

The attack could be stopped by carotid sinus pressure but was resumed soon afterwards. This occurred in a peculiar way. The sinus rhythm (rate about 100) accelerated itself until gradually the previous tachycardia was established. Later on the carotid sinus pressure was without effect.

She was given 15 grains of quinine a day for two weeks and put to bed. At the end of eight days the paroxysms became less frequent but the patient felt weak. She

improved gradually until January 10, 1926, when she again developed paroxysms of tachycardia.

An electrocardiogram taken by Dr. B. S. Oppenheimer (Figure 1) during one of these attacks in June 1926, was reported as showing a "tachycardia with a rate of 132 per minute. The T-wave is inverted in lead 3. There is also present in the third lead a single ventricular premature beat. Neither the electrocardiogram nor teleroentgenogram show evidence of myocardial involvement." In reviewing Dr. Mond's electrocardiogram of November 30, 1925 and the one taken by him on June

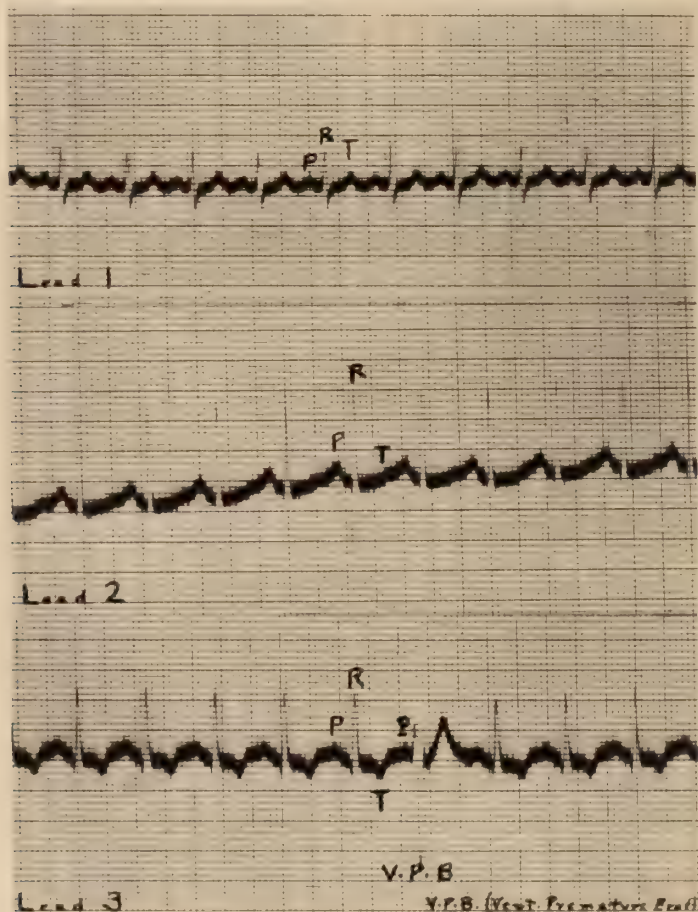


FIG. 1

11, 1926, Dr. Oppenheimer commented on the fact that "evidently foci in other chambers of her heart can also become irritable, as we have a record of ventricular extrasystoles." On the advice of Dr. Oppenheimer the patient was placed on Tr. Belladonna M. VIII. After two weeks of Belladonna she reported that while the attacks were not as severe she felt violent irregular beats.

The patient was not seen again until November 11, 1926. She stated that she was still having paroxysms of palpitations every four to six weeks, not brought on by excitement, menstruation or any obvious cause. In spite of having an easy life she

was uncomfortable because of the attacks of tachycardia as well as the premature beats which were associated with shortness of breath on exertion. Examination confirmed the presence of premature beats. Her basal metabolism was normal. She was under observation off and on for the next two years during which time she experienced recurring paroxysms of palpitations which would last from one to two or more hours.

In May 1927 her palpitation and dropped beats no longer bothered her but she was having gastro-intestinal disturbances characterized by gas, distension and generalized abdominal pains not related to meals. Pyrosis and belching were very annoying after almost every meal. She also suffered with marked constipation. Examination was entirely negative and she was given a bland diet with alkali medication. With this her symptoms were only partially controlled but she felt better and went along on her restricted menu for the next five years, until April 1933.

On April 3, 1933 she again experienced a sudden attack of palpitation followed by irregularities in her pulse. She stated that one night she was roused from sleep with a severe paroxysm of dyspnea and felt as if her heart were ready to burst, because of the rapid and violent hammering. This lasted only a few minutes. Two days later she had another attack which kept on recurring at short intervals all morning. Examination showed a pulse of 120, blood pressure of 115 systolic and 78 diastolic. The heart sounds were loud and clear, and there were no murmurs.

She returned August 16, 1933 complaining that exertion of any kind, even the act of eating, caused shortness of breath. During some nights however, she was awakened by a somewhat different sensation of air hunger, which she recognized as being due to her attacks of palpitation. Examination on this occasion was negative, except for a pulse of 108 and blood pressure of 140 systolic and 90 diastolic. Electrocardiogram showed a sinus tachycardia. She was given sedatives. On September 25, 1933 she complained that her dyspnea persisted and extrasystoles terrified her. She was nervous and slept poorly. On October 16, 1933, she stated that she was in a markedly nervous condition on account of her heart. Her pulse jumped from 85 to 100. She was unable to sleep because of the change in rate and rhythm. She also complained of severe sneezing every morning on awakening. On inquiry, she admitted that she had had this for eight years. She stated that she could sneeze indefinitely if she did not blow her nose. She suspected that foods might be responsible for this. In view of these symptoms she was referred for an allergic study.

When first seen by me on October 15, 1933, her chief complaints were recurring attacks of sneezing for many years, stuffiness of the nose and a rapid pulse. She stated that her father and a cousin had asthma. Study from an allergic point of view disclosed her to be sensitive to the following:—*Inhalants*: orris root, wool, horse dander, dust, camel hair; *Foods*: milk, asparagus, carrots, cauliflower, celery, cucumber, lima beans, onions, peas, potatoes, rice, squash; *Fruits*: apple, cantaloupe, cranberry, fig, grape, orange, peach, honeydew and strawberry; *Fish*: lobster and oyster; and chocolate.

She was placed on a diet eliminating these foods and told to avoid the offending inhalants. On this regime she definitely improved. When seen by Dr. Ottenberg on March 7, 1934 she stated that she had been on her diet since the middle of October and had had only one attack of palpitation. Her breathing was much better, and sneezing very much less, except when she used face powder containing orris root. Her pulse, which on previous examination ran about 100 beats to the minute, now was less than 80. The single attack of palpitation which she had suffered, came on in the evening, after she had drunk several glasses of whiskey. This paroxysm however, lasted only one to two minutes. Her general physical examination was essentially negative.

On December 7, 1934, she came in to see me and stated that she wanted to prove to herself that chocolate, of which she was very fond, and to which she gave a positive skin reaction, was really harmful. Three days after eating a fair amount, she developed a marked attack of palpitation approximately five to ten minutes in duration. This attack was succeeded by extrasystoles lasting about a day. She stopped eating chocolate for several weeks and felt well.

Not fully convinced as to the cause and effect she again ate some chocolate and on the same day she developed a marked angioneurotic edema of her face. This was followed on the third day by an attack of severe palpitation, lasting about five minutes. On repeated inquiry she was emphatic as to the time interval between the ingestion of chocolate and her cardiac symptoms. She stated that it took three days after eating chocolate before she developed any symptoms.

After these attempts she ceased experimenting and kept to her diet. Since then until now, June 1938, a period of approximately four and a half years, she has had no attacks of paroxysmal tachycardia, extrasystoles or any symptoms, referable to her respiratory systems, in the form of sneezing or dyspnea.

Summary, Case 2. A schoolteacher of 37, whose father and cousin both suffered from asthma, was first seen in November 1925, complaining of attacks of cardiac palpitation. She also gave a history of sneezing for many years. Because the major symptoms were referable to her heart, the latter was carefully watched for eight years and examined by means of numerous electrocardiograms and X-ray studies. The electrocardiograms on various occasions between 1925 and 1928 revealed paroxysmal tachycardia of auricular origin, premature auricular and ventricular beats with the heart rate varying between 130 and 210. Throughout these years there was no evidence of valvular or myocardial involvement. In 1928 the cardiac symptoms apparently disappeared but they were replaced by gastro-intestinal symptoms which continued on and off until 1933. On a bland diet and milk of magnesia, etc. she gradually improved. In 1933 after an interval of five years of freedom from tachycardia, a period during which her gastro-intestinal symptoms predominated, the attacks of tachycardia returned, and the gastro-intestinal symptoms disappeared. At this time she also complained of severe sneezing, which she admitted had lasted for many years, and complained of dyspnea on exertion. Electrocardiogram taken on this occasion revealed a simple sinus tachycardia. This newly elicited information suggested a possible allergic origin for her symptoms.

Investigation along these lines disclosed reactions to various foods and inhalants. Many of these could be tolerated without arousing any symptoms. The most important, clinically, proved to be shell fish and chocolate. Ingestion of either of these, was followed by attacks of palpitation and on one occasion preceded by angioneurotic edema. The cardiac symptoms occurred three days after ingestion of the offending foods. This is characteristic of the delayed reactions frequently seen in food hypersensitiveness.

Removal of the offending allergens resulted in marked improvement in

her nasal symptoms as well as disappearance of the various cardiac manifestations which (in the course of ten years) had been characterized by paroxysmal auricular tachycardia, premature auricular and ventricular beats and simple sinus tachycardia.

Case 3. History. Patient T. was first seen in 1925, at the age of 57, complaining of angioneurotic edema. She gave a history of recurrent attacks of urticaria from 1907 and gastro-intestinal symptoms characterized by colitis alternating with urticaria. At times the gastro-intestinal attacks were preceded by a sensation of choking and substernal oppression. There was no history of asthma nor hay fever. In the course of ten years contact with her family I have seen one sister, ten years younger, develop angina pectoris with coronary sclerosis and what appeared to be bronchial asthma. The asthmatic seizures occurred after upper respiratory infections and subsided after several weeks. Another sister suffers from frequent sinus attacks, and her son has had gastro-intestinal symptoms for a number of years due to food hypersensitiveness.

Examination of the patient in 1925, showed a well nourished woman, about 5 feet 7 inches in height, and weighing 205 lbs. The eyes, ears and nose were negative. There was marked swelling of the lips and right side of the face caused by angioneurotic edema. The skin was smooth and of good texture. Angioneurotic edema was present in the fingers of right hand, right foot and face. The lungs, heart and abdomen were negative.

Laboratory Data. The urine and blood chemistry examinations were negative. A roentgenogram of the heart showed slight hypertrophy of the left ventricle. The aorta was normal. The lungs showed a number of calcified nodules in the left upper lobe. An electrocardiogram showed a sinus bradycardia which was marked on vagus stimulation. The ventricular complexes were normal. The T-waves were upright in all leads. There was no preponderance. The blood pressure was 180 systolic and 80 diastolic.

Course. A study of this patient from the point of view of protein hypersensitiveness yielded a few doubtful reactions to eggwhite, raspberry and strawberry. She was placed on an elimination diet, to which she paid but little attention, and continued getting attacks of angioneurotic edema off and on every few months.

When free from angioneurotic edema her blood pressure would rise to about 200 systolic and 80 diastolic. This gave her discomfort, such as fullness in her head and insomnia. After a few days rest in bed, her blood pressure would come down to 160 systolic and 80 diastolic, and she would feel perfectly comfortable.

In 1929 after a dinner consisting of lobster and oysters, she was aroused in the early morning by a violent thumping of the heart, choking in the throat, nausea, vomiting and abdominal cramps. She was found sitting up in bed, complaining of dyspnea and precordial pain.

The heart rate was extremely rapid and very irregular, characteristic of auricular fibrillation. The rate was estimated at about 250 or more. The pulse was difficult to count, having the usual irregularities characteristic of this type of arrhythmia. This continued for about four hours. Gradually the heart slowed.

An electrocardiogram taken by Dr. E. P. Boas about six hours later revealed auricular and nodal premature beats. The heart rate was 70.

In view of the history of the eating of shell fish, she was advised to take a purgative and colonic irrigations. Within thirty-six hours she felt well again. Her heart had returned to a normal rhythm and to its usual rate of 60. Because of an idiosyncrasy to morphine, no sedatives other than bromides were given.

During the years from 1930 to 1934 she had recurrent attacks of severe angio-

neurotic edema, involving her hands, feet, lips, tongue, and extrasystoles. They always followed eating of shell fish from which she refused to abstain. As she got older, her attacks of angioneurotic edema were preceded by a sense of profound fatigue and at times by typical seizures of angina pectoris. Premature beats were frequently associated with these symptoms. During such attacks her blood pressure would rise to from 200 to 230 systolic and from 80 to 90 diastolic.

The anginal attacks came on during the night and would awaken her. One could always trace these to some dietary indiscretion committed one or two days previously. Usually it was fish or cabbage. In the intervals between the attacks she would feel perfectly well and accomplish a good deal of work. Examination of her heart during such free periods was negative, except for a bradycardia (pulse, 60).

While traveling in Switzerland in 1934 (she was then 67), she developed a severe attack of angioneurotic edema affecting various parts of her body, which lasted several weeks. Examination at that time, except for the angioneurotic edema, was generally negative as far as her heart and lungs were concerned. Laboratory examination of urine and stool was negative. Blood examination was negative except for an eosinophilia of 6 per cent.

Investigation from an allergic point of view by skin tests to a dozen different foods indicated a marked reaction to lobster. In addition, hemoclastic reactions to milk and beef suggested that she was sensitive to those foods.

After returning from Switzerland she was careful of her diet for a while and abstained from beef, milk and shell food. She found however, that she could eat milk and beef without any ill effects, in spite of the positive leucopenic index to these foods. If, however, she lapsed with regard to shell fish, she invariably developed severe attacks of angioneurotic edema with or without angina pectoris and premature contractions. During some of her anginal attacks, her liver was found to be swollen and painful. Her blood pressure at such times rose to 230 systolic and 80 diastolic. Catharsis invariably was followed by relief.

At the present writing her blood pressure still fluctuates between 165 to 200 systolic and 60 to 80 diastolic. During free intervals her heart shows no abnormalities. The rate is about 60 beats per minute and her electrocardiogram is normal. Her liver likewise is not enlarged.

Summary, Case 3. A 68 year old woman was observed first in 1925 at the age of 57, and for eleven years thereafter. Throughout these years she had attacks of severe angioneurotic edema and occasional colitis following the eating of shell fish. In 1929 after eating a mixture consisting of oyster and lobster she developed an attack of auricular fibrillation. An electrocardiogram taken several hours after the attack of fibrillation subsided showed nodal extrasystoles. Since 1930 she had attacks of angina pectoris and cardiac arrhythmia characterized by premature beats, alternating with angioneurotic edema, or angina pectoris alone, whenever she ate shell fish. When her precordial distress was severe, her liver became enlarged and painful. This was relieved by catharsis. She attributed some of her attacks to fatigue and worry. Although this was a factor at times, we found that fatigue frequently followed the eating of shell fish and was an allergic manifestation of dietary indiscretion.

DISCUSSION

A review of the clinical course of the above cases indicated that attacks of paroxysmal auricular tachycardia with or without premature auricular and ventricular beats, as well as auricular fibrillation, may occur in apparently healthy individuals who are sensitive to specific foods. The allergic origin of such attacks in our patients has been established on the basis of accepted criteria used in the identification of allergic syndromes i.e., a) the presence of family or personal history of allergy in all three cases, b) the occurrence of respiratory or other vascular allergic manifestations in the form of urticaria, angioneurotic edema, in cases two and three, c) the presence of multiple positive skin reactions in two of the three patients tested by the intradermal method, d) the identification by repeated clinical trial of certain specific foods which on ingestion would elicit cardiac symptoms, e) the complete cessation and control of symptoms by removal of the offending foods.

In surveying the English literature only two references to cases of cardiac arrhythmia, studied from an allergic point of view, were found. One of these was by Duke (1), who reported two cases, which he considered illustrative of "physical allergy." His first case of tachycardia was brought on by "heat" or "effort" and relieved by cold; the second was a hay fever patient who developed extrasystoles on the basis of cold sensitivity and was relieved by the application of heat. Kern (2) cited a case of a woman aged 40, with paroxysmal tachycardia since the age of five. Skin tests in this patient gave only slight reactions to two foods from among those which she thought to be responsible for her attacks. In evaluating this case Kern stated that he "hesitated to say that allergy was the underlying cause of paroxysmal tachycardia. It may in all likelihood be simply the spark that sets off the powder."

In the French literature there are two papers. One by Laubry et Mussio-Fournier (3) of a case of urticaria alternating with paroxysmal tachycardia and the other, a series of five cases described by Weil (4). The first of these was a man aged 35, who had paroxysmal tachycardia associated with asthmatic attacks, hay fever and urticaria; another had migraine and tachycardia; a third, eczema and tachycardia; the fourth, angioneurotic edema and tachycardia; the fifth, had digestive disorders, an emotional icterus (at the age of 13?) and tachycardia five or six times a year.

In the German literature there is a report by Luria and Wilensky (5) of the case of a Russian peasant woman of 45, who first began to have attacks of paroxysmal tachycardia once or twice a year and subsequently two or three times a week, which they were able to trace to the eating of

honey and raisins. Skin reactions to these were positive. The attacks could be elicited ten minutes after eating raisins, and were relieved by vomiting.

The striking fact in most of the cases so far recorded is the frequent presence of other allergic manifestations, such as angioneurotic edema, urticaria, migraine, hay fever and asthma. It is also important to note that in many of these patients such symptoms were not merely associated phenomena but would alternate with each other. Thus, there was from time to time a shift in the shock organ which dominated the clinical pictures. At one time respiratory symptoms would prevail as in our first and second patient, at other times gastro-intestinal disturbances alternating with tachycardia. Thomas and Post (6) reported a patient of 34 with migraine and tachycardia, without attempting to explain the underlying mechanism, and expressed the opinion that the "paroxysmal tachycardia may be the cardiac manifestations of migraine occurring in those patients and in those circumstances wherein sick headaches might occur, and may be the only manifestation of migraine, or may replace entirely the sick headache etc."

This substitution or shifting of symptoms from one group of tissues to another, may be ascribed to a temporary desensitization of the reacting tissue and a transference of the state of sensitivity to another. Reactions in the second shock organ can be induced by the same antigen responsible for the first group of symptoms observed, or to other allergens.

A possible predilection of certain antigens for different shock organs is also frequently noted. Thus, for example, in the first case, lamb would induce paroxysmal tachycardia; cabbage or cauliflower, vasomotor rhinitis and cough, whereas a combination of these would initiate first, upper respiratory symptoms followed by tachycardia. In the second patient orris root would cause sneezing; chocolate, paroxysmal tachycardia. This affinity of certain antigens for specific tissues is commonly seen in cases of ragweed hay fever and asthma, where ragweed is usually responsible for respiratory allergic manifestations rather than gastro-intestinal; also in tobacco hypersensitiveness where the cardiovascular system is apt to be affected; or in drug allergies such as phenolphthalein in which skin rather than systemic manifestations supervene.

The exact nature of this relationship is not clear. A constitutional factor may predetermine the specific shock tissue in the allergic individual. The degree of involvement may depend upon the inherent sensitivity of the shock organ and the character of the stimulus. As evident in our first case mild antigenic stimulation brought about by a meal of lettuce, tomatoes and wheat, induced only premature beats, whereas the greater sensitiveness to lamb alone, or in combination with cabbage and cauliflower invariably led to paroxysmal tachycardia. In our third patient

ingestion of a combination of lobster and oysters was followed on one occasion by an attack of paroxysmal auricular fibrillation, in another by angina pectoris and premature beats.

That cases of auricular flutter or fibrillation occur in apparently healthy individuals has been but recently emphasized in a statistical study by Orgain, Wolff and White (7). These authors collected a series of fifty-four patients, forty-seven of whom had fibrillation; five, auricular flutter; and two had both. They concluded that "auricular fibrillation and auricular flutter are in some persons merely exaggerated functional disorders of the heart, no more indicative of cardiac disease or of poor prognosis than are premature beats or auricular paroxysmal tachycardia."

Unfortunately in their studies they pay no attention to the factor of allergy. Investigation from this point of view may disclose that sensitization to foreign proteins, either bacterial, foods or inhalants play important rôles in precipitating certain cardiac arrhythmias, especially those not associated with permanent myocardial damage. At present such irregularities are rather loosely attributed to toxic influences by many clinicians who are rather wary of the concept of allergy and suspect that the word "allergy" is employed entirely too often and uncritically in explaining obscure clinical phenomena. The indiscriminate characterization of functional disturbances in various organs as due to "toxic" factors, is however to be equally deprecated. Toxicity and allergy must be clearly differentiated. The confusion which arises between the two is due in part to the fact that both may be operative simultaneously, especially where a bacterial focus is the underlying cause, and partly because of the ingrained concept that bacterial infection and toxins are the *sine qua non* instigators of disease processes.

Advances in our knowledge of bacterial hypersensitiveness have taught us to realize that there is a decided difference between toxic and allergic effects. It is well known that whereas toxins usually react on everyone, the most minute quantities of allergens, completely innocuous to the average person will not only influence some and not others, but that the same antigen may affect shock organs in different allergic individuals with the most dire results. It requires therefore no stretch of imagination to appreciate that allergy to infection may find its expression in certain functional disturbances of the cardiovascular system, just as an attack of asthma may be an expression of hypersensitiveness to infection from a focus present in the sinuses or lungs. But before we can prove that hypersensitiveness to bacterial proteins may initiate changes in the cardiovascular system, we must be able to demonstrate clinically that controllable antigens, such as foods or inhalants, can be responsible for such disturbances. We believe that our cases represent this fact.

SUMMARY

Three patients with a family background of allergy, two of whom presented the clinical picture of paroxysmal tachycardia, followed by premature beats; and one manifesting auricular fibrillation, angina pectoris as well as extrasystoles, were investigated from the point of view of hypersensitiveness to foreign proteins.

It was found that each patient in addition to the above-mentioned cardiac manifestations had other symptoms of hypersensitiveness, characterized by vasomotor rhinitis, colitis and angioneurotic edema. These were coincident or alternated with the paroxysms of tachycardia, or auricular fibrillation.

Intradermal skin tests yielded multiple reactions to foods and inhalants, in two of the patients and questionable reactions in the third.

Clinical trials with the numerous reacting substances were carried out in order to identify the proteins responsible for the symptoms. Only the ingestion of the specific foods which would elicit attacks of cardiac arrhythmia were regarded as etiologically significant.

In two of our patients such reactions would follow three to four hours after ingestion of the offending foods. In the third case they were usually manifest on the third day (delayed reactions).

Removal of the offending allergens from the diet resulted in freedom from cardiac symptoms as well as those in other shock organs in every instance without any other form of therapy being used. It may be assumed therefore that the cardiac arrhythmias in the cases under investigation were on an allergic basis.

It is suggested that this type of cardiac arrhythmias be designated "Allergic paroxysmal tachycardia, auricular fibrillation, or premature beats," in order to distinguish them from cardiac irregularities of different etiology.

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SOME OF THE PROBLEMS IN THE DIFFERENTIATION OF THE NEUROSES AND PSYCHOSES

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In the ordinary practice of psychiatry there seems to be very little difficulty in the differentiation between the neuroses and the psychoses, as society itself establishes in a pragmatic way this differentiation. Psychotic patients are people who cannot get along in ordinary community life. They are in one way or another dangerous to themselves or to others, they hold strange beliefs, they suffer from unusual experiences not shared by others; hence, society protects itself from such people by isolating them or by insulating society from them. The people who are neurotic are commonly recognized to be suffering from symptoms which strikingly resemble the symptoms of ordinary physical ailments. The emotional life of such people is not too distant from the experiences of the average man, hence, the attempt is made to consider such people as suffering from some obscure physical ailments and treat them along orthodox medical lines. If society at large makes such a classification, the psychiatrists themselves have done comparatively little to change it. This probably accounts for a good deal of the retardation of the progress in psychiatry as a medical science. There are, of course, powerful reasons why this course has taken place. The psychiatrist likes to think in terms of clinical entities because in his medical education he is taught to think in such terms and a great part of the clinical teaching is devoted to the problems of the differential diagnosis between various clinical groups and sub-groups. What is more important, the thinking in terms of definite diseases convinces the psychiatrist that psychiatry is really a medical science; consequently the methods of investigation, and, what is more important, the solution of psychiatric problems lie within the scope of research methods applicable to all biological sciences. In spite of the fact that the psychiatrist himself may come to the realization of the importance of the early environmental factors of the etiology of the psychoses, as well as the significance of social and economic stresses, he approaches psychiatry not from what he knows from his experience, but from the purely medical or biological point of view, which gives him the conviction that in working with psychiatric cases he remains essentially a physician. This undoubtedly is very useful, as it gives confidence, as well as a method of attacking problems in psychiatry which still has numerous possibilities. On the other hand, the forcible squeezing of cases into mythical homo-

geneous groups results only in invalidating nosological attempts and discouraging any attempt at classification. The fact that present nosological groups lack fundamental objectivity can be illustrated by the frequency with which diagnoses are changed when the patient is transferred from one State hospital to another (1). The fact that psychoses can at the same time show dissimilar clinical pictures largely depending on the emphasis and the interest of the psychiatrist is well illustrated by Campbell (2). On the other hand, Malamud and Lindeman (3) have pointed out that even in the course of a fairly typical psychosis there are certain phases when the clinical picture is quite different from the predominant psychosis which the patient presents. Thus, in a series of affective psychoses, they have shown how in the early phase one deals either with a fairly characteristic schizophrenic picture or with one that is altogether atypical. I myself have demonstrated cases where one could not differentiate between such fairly opposite entities as manic depressive psychosis and schizophrenia (4). Adolf Meyer called attention a long time ago to the fact that one should study the content of the psychosis rather than worry about nosological differences. The present confusion in nosology is probably due to the fact that the patient in distress is not interested in following any arbitrary classifications but tries to solve his difficulty in a variety of ways with the rapid succession of various types of solution, producing dissimilar phenomena, depending upon the phase in which the patient is studied. It is quite certain that the psychotic patient attempts at first to solve his problems by means of a neurosis and only much later accepts a different solution when the neurotic repression gives him no relief. This was well pointed out by Sullivan (5) who called attention to early symptoms in schizophrenia when the patient complains of a great number of bodily symptoms without resorting to any dereistic thinking or delusional formation. All this, however, should not interfere with the attempt of the psychiatrist to recognize on what level the patient is attempting to solve his difficulties and with what success. The author's present interest lies in that intermediary stage where the patient is not able to solve his difficulties by means of a neurosis and yet has not developed a full-fledged psychosis as a complete solution. Curran (6) in a recent study attempted to differentiate between the neuroses and the psychoses limiting himself to such dissimilar pictures as those found in the neuroses and manic depressive psychoses. His differential criteria are as follows:

<i>Psychotic</i>	<i>Neurotic</i>
1. Presenting subjective complaint of depression.	1. "Anxiety" or "fatigue."
2. Somatic complaints absent or unimportant.	2. Prominent.
3. Remorse and self-reproach present.	3. Absent or "insincere."

Psychotic

4. Does not blame others.
5. Loss of weight "invariable."
6. Constipation "invariable."
7. Depersonalization present.
8. "Adequate" precipitating factor often absent. "Cause" often not discoverable.
9. Steady course "strikingly independent of environment."
10. Healthy except for circumscribed attacks.
11. Positive family history

Neurotic

4. Blames others.
5. Not invariable.
6. Not invariable.
7. Absent.
8. "Adequate" precipitating factor often present. "Cause discoverable or clear."
9. Unsteady variable course, dependent on environmental factors.
10. "Seldom absolutely well."
11. Negative family history.

Reviewing his clinical material on the basis of these differential criteria he comes to the conclusion that almost every conceivable mixture is to be found in these two frequently contrasted types of reactions which at the present are only distinguished for the purposes of clinical convenience. If such difficulties exist in differentiation of the atypical cases of psychoneuroses and affective psychoses, there is even more confusion when it comes to differentiation between the neuroses and early schizophrenia. Here a notable service has been performed by Nolan D. C. Lewis (7) in his attempt at differentiation, which takes into consideration not only the superficial symptoms of the clinical picture but also the fundamental dynamic drives of the patient. He differentiates the two as follows:

Psychoneurosis

1. Personality relatively intact.
2. Primary disorder in "free floating" affect anxiety. Quantitative exaggerations of normal emotions.
3. Anxiety always present in some form: emotional uneasiness, feelings of insecurity and fear, but no real associated delusions or hallucinations.
4. Physical discomforts: sensations, pains, constrictions—rationally but incorrectly explained.
5. Dissociation: practically none except in hysteriform components; some benign feelings of unreality or delusions against others.

Dementia Praecox

1. Transformations of personality relatively common.
2. Primary disorders in association of ideas and affectivity disjunctions. Qualitative changes in emotional expressions. Emotional distortions.
3. Anxiety present at times, but often disjuncted from reality or falsely interpreted—may be connected with tormenting self-reproaches and self-accusatory delusions—sense of guilt more consuming—anxiety often caused by hallucinations.
4. Hypochondriasis more dominant and bizarre—often explained in delusionary manner.
5. More marked loss of borderline between reality and unreality; more definite feelings and convictions of unreality in self and outside world.

Psychoneurosis

6. Projection elements or delusions against others mild, and in connection with more or less real misunderstandings.
7. Obsessive thoughts—invading ideas which displace and contradict the usual preoccupations of the subject—produce “intellectual vertigo” (fear of loss of all reason—differentiate from physical vertigo which gives the impression of imminent death). Feelings of compulsion to do things.
8. Hallucinations rare. “Expectation” hallucinations or rather “illusions” may be more active than normal.
9. Psycholeptic attacks—seen in psychasthenia. Severe disorganizing, confusing anxiety attacks may be followed by some depression.
10. Suicidal reactions more apt to be “gestures” to gain attention.
11. Intellectual disorder—disturbance of mental content and lack of concentration because of divided attention (one part on personal troubles—other on thing at hand)—causing temporary disturbance.
12. Insight retained.
13. Retention of ideal of ego. Retention of the point of view of society and of previous training.
14. Progression to states of more complete invalidism.

Dementia Praecox

6. Projection with lack of insight more active. Deeper seated and often absurd delusions against others.
7. Obsessive thoughts more apt to “be shared by others” or controlled by outside forces (difference in insight). Indicates loss of borderline between reality and unreality. Feelings of “mind being read” and of “thoughts known to others.”
8. Hallucinations may or may not be present, but when present and associated with mystical interpretations, feelings of mind reading, etc., they at once indicate the diagnosis (particularly if a comparatively new development).
9. Accompanied by bizarre ideas, vagueness of thought, indecisiveness, somatic delusions, and paranoid projections—followed by deep depression (agitated form) and suicidal reactions.
10. Suicide more apt to be genuine and successful.
11. Intellectual disjunction invariably present because of deeper split in personality—with depersonalization—some things done well—memory disturbance as such varies from none to complete loss.
12. Insight usually impaired.
13. Beginning loss or disturbances in ideal of ego. Loss of social sense and habits.
14. Progression of mental oddities by increase and shifts in the picture. Finally deep regression to “vegetative” level.

The difficulty in understanding at which level the patient is attempting to solve his problems or rather the intermediary level at which they were found when they were studied by me can be illustrated by the two following cases:

Case 1. A. B., female, single, age 32, white, clerk.

The patient was referred to the psychiatric clinic of the Michael Reese Hospital by the Leahy Clinic in Boston. When the patient entered the room one saw a well

developed, well nourished, rather stocky, masculine-looking young girl with a constrained, labored expression on her face. She spoke in short, gasping sentences and stated that she was tired of being tossed from pillar to post by people who found her requests unusual and tried to dissuade her from doing what she wanted to do. The patient stated that she was well until three months ago when she left her job as a clerk because she felt that she needed an operation. For a long time she had been disturbed by the fact that she had large, pendulous breasts which seemed to her ugly and disgusting. She went to the Leahy Clinic asking if the removal of the breasts was a serious operation and received the reply that it was a very simple and not dangerous procedure. She went there and the report from the clinic stated that the general physical examination as well as a neurological examination proved to be entirely negative. "The patient's main reason for coming to the clinic was that she wished to have her breasts removed. The examination of the breasts revealed that there was a definite mastitis, but in view of the mental situation we all felt that any surgical procedure was hardly warranted. The history regarding her attitude concerning the breasts I am sure you have been able to obtain with much more detail than we did. The girl had rather an unusual life and there was a homosexual trend running through her story." The patient's request and her attitude were so peculiar that the psychiatrist in the clinic advised the patient to return to Chicago and see us.

Upon further questioning the patient stated that she had a very serious reason for wanting to have her breasts removed. She stated that three months ago she fell in love with one of the girls in the filing room of the place where she works. This girl had been living with a well-known Lesbian for the last six years. In spite of this the girl was willing to have an affair with the patient. The girl was very charming, beautiful and had very pretty breasts. Patient felt that she could not possibly have an affair with this girl when her own breasts were so ugly. This gave rise to her desire to improve her appearance before starting the affair. She was so upset by the girl that she had to quit her work as she was too love-sick. The patient stated that she never was in love with a man, although she was curious and various times she allowed men to approach her but they always disgusted her by the expression of animal passion in their faces when they became aroused. The patient stated that she had crushes on girls ever since she can remember and that the most attractive things about girls were their breasts. There had been very little overt homosexuality in a sense of sexual intimacy. The patient stated that technically she was still a virgin. The patient herself always wanted to be the initiator, the aggressor, and she did not like girls who became sexually aroused when she was with them. Some time ago she spent the night in New York with a girl who knew various methods of sexual gratification and she became so disgusted with her sensuality, her passion, and the fact that she was taking the initiative that she terminated the affair. The patient stated that nothing would please her more than to have a girl of her choice to live with and that she, the patient, would do all the outside work, provide for the "family" and take full responsibility.

At the second interview the patient stated that she wanted to be analyzed, and that was why she had come to see me. She demanded that the analysis should start immediately but stated that she did not want to pay for it or make any sacrifices for it. She could think of many ways in which to spend her money rather than for being analyzed. She liked nice things, comfort, good food, etc. She showed me a letter from a friend with whom she had had an intimate, long relationship in college, who strongly urged her to be analyzed and who promised to pay some of her expenses. The patient stated that she was willing to accept this help but that she felt the fees of the analyst were exorbitant; she felt the analysis should be done for practically

nothing and in this respect her attitude was not one of asking for help but one of demanding, insisting, mixed with a good deal of hostility and aggression. At my request she had prepared an outline of her life which she brought with her. She stated that writing things out helped her to see the connection between certain things and the development of her homosexuality. When the patient was asked if she wanted to be cured of her homosexuality she stated there was nothing to be cured of and that she did not consider this as a disease.

The patient's written account of her life was a volume in itself which was written in very clear, fine longhand. In this she went over very carefully her recollections from the age of five through her high school years. Some of the material in this account showed the factors contributing to the development of the patient's homosexuality as well as some of her fantasies.

"Five years old. My favorite playmate was Virginia, a child of my own age, who lived next door. She was an only child, carefully reared, whose parents were people of some refinement. The amusement from which Virginia and I derived most pleasure was spanking each other; though not hard enough to cause pain. One day, when we were so engaged, my mother entered the room and remarked, "That isn't a nice way to play. Nice girls don't do that." When free of her presence, we continued to amuse ourselves as before, only now with furtiveness, a secret sense of guilt. I received more pleasure in spanking Virginia than in being spanked by her. The idea of the spanking game originated with Virginia. At first I had thought it silly, but in a short time came to like it.

"Virginia's bedroom and my bedroom were separated only by a narrow courtyard which ran between the apartments. Virginia used to lie on her bed, I on mine, and Virginia would pretend that she was crying because she was being spanked. I cannot remember whether I, too, pretended I was being spanked; but I do remember I did not pretend I was crying. Virginia's loud outbursts seemed to me somewhat shameless; they embarrassed me.

"One evening, when Virginia and I were in her backyard, her father snatched her off the ground, put her across his knee and pretended to spank her. She laughed. Then her father, thinking no doubt that I might feel slighted, tried to put me across his knee. But, although I knew he did not intend to hurt me, I became terrified and began to scream. I kicked and scratched him until released and never went near him again."

This last memory of being spanked by Virginia's father probably played an extremely important part in the patient's homosexual development. It is quite obvious that the patient equated the spanking with sex and the idea of intercourse was always in her mind connected with an extremely brutal, sadistic image of a man whipping a little girl, an image so horrid that the patient could never allow herself to accept herself as a woman.

"On the fourth of July my father brought home a big basket filled with all sorts of fire works—sky-rockets, shooting stars, and kinds which the other children did not have. Since he was afraid to let me shoot off the fire works, two older boys in the neighborhood were asked to shoot them off for me. They, in turn, asked several of their boy chums to share the fun. I hated all these boys; they were stealing what was mine. 'Just wait,' I thought with burning resentment, 'Just wait—when I'm older I'll show you, old William 'n Edson.' I never forgot this and continued to hate these boys."

"Until I was eight years old, I liked my Aunt Annie best after my father. She was my father's unmarried sister, a very beautiful young woman of 30, attired always in elegant, sweet-smelling clothes. She always dressed my dolls and embroidered blankets for my doll's bed. I considered her ever so much nicer than my mother and was very proud of her beauty. She didn't look like an aunt at all, but like a girl, I

thought. When left with my grandmother in Annie's absence, I would lie down before the front door and cry myself to sleep. My grandmother, an old, wrinkled woman with a sharp tongue, frightened me. I was afraid to be alone with her.

"The only time Annie ever frightened me was when she attempted to administer an enema. She removed my drawers and placed me over her knee, then inserted the rubber tube. I squirmed until she let me down. A feeling of shame, the first of which I was conscious in my life, was mixed with the fear."

At the age of eight the patient recalled how her mother taught her cleanly habits which she learned to practice automatically without thought. She stated that at this time she never touched her genitals, did not know what her body looked like, and had no curiosity about it. Neither did she have any curiosity about her brother. But at the same time the patient revealed tremendous interest in little baby girls as revealed in the following note:

"It was not curiosity that led me to undress Antoinette's baby sister, Mildred, under the back porch whenever no one else was present. I wanted only to stroke her soft skin. I never had an impulse to kiss the child, nor did I touch her genital organs—did not even notice. But the velvety softness of her cool skin gave me great pleasure. I was always very gentle whenever I undressed the little girl and was careful to see that no one was near. This practice of mine was never discovered. The child liked me and never cried out, nor told her mother."

Also at this age the patient gives her family constellation which consisted of her father, her mother and the brother three years younger than she was. It was also at this age that her father was killed in an automobile accident. "I could not believe that my father was really dead, therefore felt no grief. The crying of the grown-ups annoyed and embarrassed me. When I heard that my father was dead, I went into the bathroom, locked the door, and stretching on my tiptoes, looked closely at my face in the glass the first time in my life. I bulged out my cheeks and twitched my nose to make certain I was alive, that it was all true; I made my mouth smile into the glass. They wanted me to kiss my father's forehead when I passed by the casket but I was afraid. I was called an 'unfeeling child' because I did not cry. It was only at night in bed that I ever did this.

"For many years I dreamed at night of my father, so vividly, that when I awoke in the morning I could not believe he was not there in the house with us. For many years I expected him to return. I never really believed he was dead, although I had seen him lowered into the earth and went often to put flowers on his grave with my mother."

At the age of nine the patient revealed her extreme attachment to her teacher, which largely expressed itself in mute admiration with the tendency to do minor errands for the teacher. At the age of eleven was the only time when the patient began to have any mild affection for a man.

"*Eleven Years.* We now had our own apartment, which a young man cousin, John, shared with us. I was very fond of John. He is the only man on whom I have ever desired, consciously, to make a good impression. He was 27 at this time, very moody, sarcastic, bitter, had spent two years in reform school. He had a sweetheart, about whom I liked to tease him. I used to sit on his lap and take pleasure in annoying him. He disliked children, never gave me presents at Christmas, and taunted me about the failure of my baseball team to win even one game from another school. He was studying art and had unconventional opinions of many matters, especially war. Today he is still the only man who has ever interested me. I find it faintly exciting to sit at family dinner with him. He is married (to the sweetheart) and has two children, ages 15 and 13. I am able to sit and talk to him with pleasure, mostly about modern art. I am conscious of myself as a woman in

his presence, and in his presence only. This consciousness is exciting though I do not admit it even to myself. He thinks I consider myself 'superior' and when I make an excuse to leave the gathering early, he remarks sarcastically, 'Well, you've held up nobly. Don't see how you ever stood us this long!'

"My cousin, John, occupied one bedroom, while my mother, brother and I occupied the second. My mother slept in the middle of the bed, my brother and I on each side. Sometimes my mother did not come to bed until later and my brother and I were left alone. This part is vague; but I have the impression that my brother and I drew close together and that I experienced a faint pleasure in the contact. We never touched each other with our hands, but merely lay very close together; I upon my left side, he upon his right. When we heard my mother coming, we drew apart in haste, not because we felt we were doing wrong, but because my mother had made it clear that we must stay on our own side of the bed. For some years, at night, between the ages of 22 and 28, I dreamed of my brother with pleasure; never any other man, always my brother. When I am actually *with* my brother, however, I never think of him in any way except that of a sister.

"I enjoyed spanking my brother, sometimes hurt him. But he was a gentle, good-natured boy and bore it without betraying me to my mother. I liked to do this best when he wore only his nightgown for then I could feel the flesh more clearly. We were very careful to keep this sport from my mother. I never let my brother spank me and he never cared to do so.

"Many of the boys called my brother 'pansy' because he was so gentle; I knocked some of them down for making him cry. He himself would never fight them. I had no fear of the boys and could 'lick' any boy my own age."

At the age of 13 the conflict becomes more acute than ever as evidenced by this paragraph:

"I was to represent 'pork' in an agricultural playlet given at school. For my costume I rigged up my brother's overalls, a cap and one of my brother's blouses. My hair was combed back severely so that it looked like a boy's. When I appeared in this outfit, whistling, barefoot, several of the girls looked astonished, then remarked, 'Oh but you make a cute boy!' I wished that I might always dress as a boy. I was full of self-assurance, lost temporarily (for most of that evening) all my shyness. The pride which I had in myself made me feel splendid. I swaggered."

The mother was very anxious to make the girl sociable, friendly, to mix better with other children, all of which intensified the patient's aloofness, withdrawal and extreme misery in the company of others. The mother and the patient had violent quarrels about the patient's lack of sociability. The patient's only outlets were the attachments to the older women teachers in her school, with every possible attempt to show them her affection. Her class-work, however, was excellent and she showed a good deal of talent in English, especially composition. However, even this reflected the patient's difficulties.

"At home I wrote some things which were not 'stories.' The reason for my writing what I did was that I received a queer, painful but rather delightful sensation in my stomach and genital organs. I never touched these organs with my hands, but received pleasure only by the indirect method of writing. I was the man about whom I wrote, and imagined myself to be spanking a girl of sixteen or so, clad in a nightgown. This chastisement was given in punishment, according to my written version, not in amorousness. I had never heard of the sexual act. I never imagined any love scenes between men and women. Often I would write something of this sort merely to experiment, to see if the queer, painful sensation would return. It always did. Sometimes the pain did not cease for ten minutes. I could not understand why I had such a sensation, did not have any idea of the meaning of it. I was

twenty-three years old before I was *told* what the sexual act was; no instinct had ever taught me. I was twenty-six years old before I experienced a satisfactory orgasm."

The graduation from high school was a source of great misery to the patient, as can be seen from her account of the preparations for her commencement.

"I did not wish to graduate in public with my class but decided I would rather receive my diploma privately. My mother insisted, however, that I take part in the graduation exercises. She bought me a filmy white dress for the occasion—a dress which I wore only once. I felt ridiculous in it. Everyone was accustomed to see me in middy blouse and tailored skirt, with straight hair and flat heels. When I appeared in my new outfit, with high-heeled white pumps, wavy hair, carrying a corsage, the girls nearest me looked astonished and said, 'Why, how *nice* you look, Annette!' I thought to myself savagely, 'You rotten hypocrites. *You* know I look like hell as well as *I* do.' But I remained silent. Everyone considered me a meek creature. When I became angry, I did not show it by hot words. I said nothing, but became so sick at my stomach that I could not eat for some time. When the first attack came, my knees felt as if they were ready to crumble; I lurched for a moment like one intoxicated. When I laughed, which was often, I had a tendency to become hysterical; the same weakness was felt and I experienced difficulty in sitting or standing upright. Even if I did not actually laugh, but felt only a strong inward amusement, I had the same weakness in my knees and my spine. My goiter had increased in size."

In her freshman year in college the patient developed a crush on the professor of English, a woman of unusual brilliance and intelligence. She also became friendly with one of her mates and this friendship eventually developed into a strong homosexual relationship which lasted for several years. However, a good deal of this was on a platonic level without very much overt expression.

"All through the fall I slept with her in the same bed without touching her, or feeling any desire to touch her. We would talk late into the night and in the morning all my muscles ached. She was very different from Emily—intensely sympathetic, warm-hearted, generous, magnanimous, the kindest person I have ever known. When her mother would enter the room in the morning to put down the window, I would complain in all sincerity, 'I *wish* Helen would stay on her own side. She's always coming on *my* side.' At the end of that semester, in late January, 1927, I touched her for the first time. There was a rent in her nightdress, into which I playfully put my hand. The softness of her skin was thrilling. From then on, I looked forward to embracing and caressing her at night. I had never kissed a woman, did not know how. It was she who taught me. During all the time I knew her, I never touched her genital organs—did not know the least desire to do so. Nor did she touch me. I was always the aggressor. The women whom I have loved since that time have always been compared in my mind with Helen—to the disadvantage of the former. I cannot be excited by any woman who lacks Helen's bodily characteristics—a small waist, firm, well-shaped breasts, a soft, supple skin without hair. She was entirely passive, but received as much pleasure as I from the caresses. She once remarked that my technique was far more pleasing than that of the *men* she had encountered. This I considered a great compliment. I was not jealous of the men she knew, but of the women. Men were labeled in my mind as 'only' men. One could not be jealous of a mere man; he was not important enough. Men were good scouts, very convenient to have around sometimes (to chop wood, or fix the furnace), but they didn't really count; they were not actually *people*."

At the age of twenty-two the patient was forced to leave college and came to a large city where she began to work as a clerk. She continued some contact with her friend in college, but gradually this friendship became less intense and after a period

of a few years the patient's friend became interested in a man, eventually became engaged to him and married him. The patient's friend came to see me in reference to the patient and told me that she felt for several years that the patient was a distinctly peculiar girl, that there had been a definite change in her personality and that she was terribly concerned about her as she could see the change going on in the patient without being able to help her. The friend was only too anxious to help in any way she could for the patient's treatment. Arrangements were made for the patient to be analyzed at the Institute for Psychoanalysis and she went there for three months. However, all through the analysis she brought comparatively little unconscious material, was definitely antagonistic, critical, felt that the analysis was attempting the impossible and after twelve weeks' trial she gave it up completely. I see the patient occasionally and she presents the same odd appearance of an extremely withdrawn, aloof person who if seen on the wards of a mental hospital would be immediately spotted by every psychiatrist as a typical schizophrenic.

Case 2. C. D., female, age 27, white, clerk.

The patient was referred to the psychiatric clinic by her family physician because for some time she had been complaining about the two sides of her face being different. In spite of the assurances of the physician to the contrary, the patient maintained this was so. Recently the patient desired to go to a plastic surgeon to have the two sides of her face "equalized."

The patient was the third of five children, being preceded by two older brothers and followed by a younger sister and a younger brother. The patient's early development was normal. She had a good deal of difficulty in school and the patient's mother had to see the teacher constantly as she was not able to get along there. She was difficult to manage, refusing to obey rules, etc. At the age of fifteen the patient thought that her hair was falling out and consulted a physician. She never had any friends, but during her grammar school years she was chummy with one girl. She had always been extremely attached to her sister who was a year younger and had always been more attractive than the patient. The patient was quite frankly envious of her, as the family always preferred the sister. After her graduation from high school the patient immediately secured work and had been working ever since.

She changed jobs fairly frequently. The last few years she had learned typing and, with the help of her younger sister, was able to hold her job. The sister stated that after graduation from grammar school it was noticed that the patient became interested in other girls. Going to work in a street car, the patient would stare at a very attractive girl from her own neighborhood. She stared at this girl so much that the latter became annoyed and complained about her behavior. The patient retaliated by slapping the girl's face. The sister had noticed that while riding on a street car the patient frequently stared at pretty girls "just like a man would stare at a woman." However, she did not make any overt advances to girls. Recently she had told her sister that she knew it was not right for her to be interested in girls as much as she was. She was an extremely shy and withdrawn person, had no friends and no interests. She stayed at home all the time, read very little, but listened a great deal to the radio. She was extremely devoted, however, to her younger sister and often talked about going into business with her and planning her life with her. The patient was frankly jealous of her sister's friends and had no use for them. Occasionally the patient had dates with men which were arranged for her by the sister. She seemed to be physically attractive to men but very quickly lost interest in them. She was a good scout and "kidded" around when in their company. Ever since childhood she had exhibited a rather peculiar behavior. She had always been too out-spoken and frank and had never agreed to take advice. She was constantly

under tension, was impulsive, "nervous" and quarrelsome. She became very excited when bits of news were related to her, especially stories about illnesses, deaths or operations. The two older brothers were quite distant from the patient and had no interest in her. The patient was extremely fond of her younger brother, although even with him she had a good many quarrels.

Examination. The physical examination showed evidences of an old chronic psoriasis. The neurological examination was entirely negative.

Psychiatric Examination. The patient was a friendly, pleasant young girl who spoke in a pathetic voice and asked to be helped in her difficulty. She insisted that both sides of her face were different and tried to explain to me that the left side of her face is a "good" one while the right side of the face is a "bad" one. When she turned to people the left side of her face she made friends; when people looked at the right side of her face they became her enemies. This feeling the patient had had since the age of fourteen. She did not think that anybody talked about her, but she felt that the whole world was oriented toward her, depending on the side of the face which she showed to them. In her office she had to sit in a corner so that the right side of her face was toward the wall and the left side faced the public. Several times she had to change jobs because she was moved from the corner of the typing room to the center where people could see the right side of her face. Immediately everybody became unfriendly, even hostile, and for this reason she had to leave several excellent positions. When the patient was seen a week later, she still maintained the same ideas. "I'm one-sided. I am afraid a person will see the other side of me. I know there is something there. I leave everything to you."

In going over her childhood, the patient related most extraordinary experiences as a child. She maintained that she had had sexual relations with her older brothers between the ages of seven and thirteen. She maintained that many times the brothers not only approached her but also the younger sister. The mother was aware of it, but being very tired and not being able to handle the rough, older boys, she let matters go. It was only when the patient became adolescent that the mother insisted that the boys should leave her alone. In subsequent interviews the patient brought out the fact that even her own father and uncle tried to have relations with her. The patient stated that she asked her father if he tried to have intercourse with her younger sister, and he had said that he would.

All this was taken to be a fantasy, but the younger sister gave substantially the same story and recalled that both she and the patient were molested in their childhood by the older brothers. She did not mention anything, however, about the father or the uncle. For a more thorough study of the case the patient was admitted to the hospital.

There the patient brought out the fact that ever since adolescence she had had a definite predilection for girls and felt more comfortable in their presence. She was so horrified at the idea of sex with men on account of her early experiences that she could not accept any man. The patient stated that she felt that she was a Lesbian. The patient admitted that she was definitely withdrawn from people as she felt that she was different from everybody and that she could not stand any crowds. In talking about her face the patient expressed the idea that one side of her face, the right side, was more coarse and rough than the left, apparently taking the right side of the face as masculine and the left as feminine.

In subsequent interviews the patient continued dramatically to emphasize the differences between the two sides of her face and demanded surgical intervention. At the same time she was unusually free in talking about her early experiences, spoke about her disgust with men and her hate for them. The patient spoke about a voice within her telling her to do certain things or not to do them and threatening that

something would happen if she did not do them. When an attempt was made to find out what this voice was like, it seemed more like an obsessive thought than a real voice. For over a year the patient was bothered by obsessive thoughts that she must or must not do certain things. The patient maintained that her feelings were rather those of a man than a woman. She could not imagine how anyone could love a man, but she understood perfectly well the feelings of a man who loved a woman. The patient brought out an incident in her early childhood which was apparently a screen memory. She remembered a little girl to whom the girl's brothers did the same things as the patient's brothers did to the patient. They forced her to have intercourse with them. She imagined the little girl on the top of another girl.

In her childhood she was a "tom boy," used to be friendly with boys—ran, swam and fought with them, was interested in athletics and continued to be so until the age of fourteen when all this stopped very suddenly on account of the following episode. One day she was looking in the mirror and powdering her nose when she suddenly discovered that the left side of her face was different from the right. There was a little bony prominence on the right side of her nose, the right cheek sagged, etc. The patient spoke about electrical sensations going through the right cheek, and in various ways tended to divide everything in the world according to the right or left. The patient stated that the right side of her face was more masculine than the left. She liked her mother more than she liked her father. The patient stated that it was only her face which showed this asymmetry. The rest of her body was perfectly feminine and beautiful and the patient stated that she would have liked very much to be feminine. She stated that she resembled her older brother, Harry, who was a few years older than she was and with whom she constantly picked quarrels because both of them were stubborn and wanted to have their own way. Relatives used to tell her that she and Harry seemed more like twins because of their resemblance. The patient's menses began at the age of thirteen shortly before the episode with the mirror. The onset of menses was quite a shock to the patient.

Up to the age of thirteen the patient obviously fancied herself a boy and the onset of menses was a severe narcissistic blow to this idea. It was at this time that she saw in the mirror that the two sides of her face were different, that one was more masculine than the other, and thus dissociated this part of herself. It is quite possible that the right side of her face represented the brother Harry with whom she was so closely identified and who resembled her like a twin.

In spite of the fact that intensive work was done with this patient, she maintained a very rigid attitude, demanding an operation and finding no sense in any psychotherapy. After the two weeks' residence in the hospital, the patient left and returned to the clinic only once. Three months after the patient left the hospital we were quite surprised to learn that the patient had completely suppressed her complaint of the two sides of the face being different. For the first time in her life she was also able to go out and get a job on her own. She refused, however, to maintain any contact with the psychiatrist and in general she has been as seclusive and withdrawn as she was in the past few years.

COMMENT

In the two cases presented we can see the gradations from a homosexual neurosis to schizophrenia and although Lewis' differential criteria can be of help to us in the second case, it can hardly be of much use in the first. The first case impressed me in the beginning as a somewhat unusual hysterical reaction in a homosexual girl, until discussion with a group of

psychiatrists* with a different background brought out the fact that I had overlooked a factor which should have been apparent to me in the beginning. The patient's bizarre appearance, her inability to accept a homosexual relationship which should have been preeminently satisfactory to any ordinary neurotic homosexual, her requests to have her breasts removed which was so akin to the bizarre castrative drives which a schizophrenic acts out rather than dramatizes—all these should have indicated to me the so-called malignant features of this case. One's experience with mental cases in a state hospital may occasionally preclude recognition of a serious personality involvement when it occurs in a setting which is different from that to which one is accustomed and when it is not accompanied by certain features which one usually sees in mental hospital patients. It is obvious that many such cases are present in the community, unrecognized and probably never institutionalized, largely because they do not express ideas which are essentially schizophrenic, and especially because they are without any serious behavior involvement. In the second case, we were dealing with a reaction which was more easily recognizable as schizophrenic. To Dr. Paul Kramer who was working with me on this case I feel obliged for pointing out the following malignant features:—

1. The patient's absolute inaccessibility to a discussion of her symptoms
2. The suggestion of a voice talking within her, although not possessing all the attributes of a real authority hallucination.
3. The conspicuous freedom with which the patient spoke about early incestuous relations and the clarity of her memory on these points. (In a normal person one would expect a rather complete amnesia and repression of such experiences.)
4. The patient's already advanced ambivalence and dissociation with the description of the right, or bad side of her face, contrasted to the left side of her face which was friendly and pleasant. Bleuler in his description of the symptoms of schizophrenia cites a similar case.

The important thing in these two cases, however, is the fact that in neither one of them is the clinical picture sufficiently clear to make a definite diagnosis of a neurosis or schizophrenia. We are dealing with two homosexual girls who in the first place never could become completely overt homosexuals and in whom the homosexual attempts did not solve their fundamental problems. It is very interesting to note how, in the second case, the patient for a whole year tried without success to overcome her difficulties by developing an obsessional neurosis with compulsive thoughts telling her what to do and what not to do lest some harm might come to her or others.

In both girls there was a healthy anlage of a positive oedipus fixation which was disturbed and thrown out of balance by unfortunate early

* Drs. L. Blitzsten, H. S. Sullivan and others to whom I am extremely grateful.

experiences. Heterosexuality became synonymous with fear, cruelty and pain, from which the patients attempted to protect themselves by building up homosexual defenses. These were so unsatisfactory that they did not even provide the compensations found in an ordinary neurosis so that the patients had to resort to more individualistic, and for this reason less intelligible, solutions. It is at this point that we found our patients, at a time when the whole world lost meaning for them and when more primitive infantile modes of thinking, feeling and acting assumed their ascendancy, giving a peculiar quality to the whole feeling tone of their interpersonal relations, which is vaguely described as schizophrenia (8). When we know more about schizophrenia we will also learn why and in what cases a neurotic solution is unsatisfactory, and what are the causes which determine the success or failure of such reactions. It is only then that we will be able to provide a solid foundation for mental hygiene, as we will know the precise factors which contribute or detract from the development of a psychosis.

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A CASE OF HODGKIN'S DISEASE WITH COMPRESSION OF THE SPINAL CORD, FOLLOWING TRAUMA TO THE BACK

MEDICO-LEGAL CONSIDERATIONS

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The following unusual features justify a detailed description of a case of Hodgkin's disease which was recently under observation on the Neurological Service of The Mount Sinai Hospital: 1) The rapid course of the disease; only sixty-three days elapsed from the appearance of the first symptom to the patient's death. 2) Symptoms of compression of the spinal cord, appearing two days following a relatively slight trauma to the back, right shoulder, and calf of the right leg, were the first clinical manifestations of the disease. 3) The limitation of the characteristic lesions of Hodgkin's disease to the following structures: the spinal dura, two thoracic vertebrae, the prevertebral fascia, one tracheobronchial gland, and the hilar and inguinal glands.

CASE REPORT

History (Adm. 385841). A married man, aged 49 years, a janitor by occupation, was admitted to The Mount Sinai Hospital on September 24, 1935, complaining of weakness in both legs of nineteen days' duration, inability to walk and urinary incontinence of eleven days' duration. His wife had given birth to six children, all of whom were living and well. The patient smoked moderately and drank a bottle of beer a day. He had a hernioplasty in 1911 and an appendectomy in 1914. At the age of 22, he had a penile lesion which was diagnosed a chancre but he received neither intravenous nor intramuscular treatment. The penile lesion was associated with a balanitis and swollen inguinal glands which were incised and drained.

The patient was in good health until September 2, 1935, when, while pushing a wheelbarrow filled with coal along a plank, the wheelbarrow "ran off" the plank and he fell into an underlying excavation about three feet deep, with the coal falling upon him. During the fall he bruised the right shoulder and sustained a few slight abrasions on the right calf. Although his "right side felt sore" he was able to climb out of the excavation unassisted. He finished the day's work and performed his usual duties during the next two days, at the end of which time he found that his gait was unsteady. He then consulted a physician who gave him "several light treatments" with no improvement. He remained in this condition until eleven days after the accident, when there developed gradually increasing urinary retention and severe constipation. Five days later walking became impossible and there appeared urinary retention with overflow incontinence requiring frequent catheterization.

On September 18, 1935 he was admitted to a hospital where examination disclosed

the following: right pupil smaller than left, both pupils reacting well to light and in accommodation; absent abdominal and cremasteric reflexes; exaggerated patellar reflexes (no record of the condition of the Achilles reflexes); bilateral Babinski; loss of painful, thermal, and tactile sensibility on the outer aspect of both legs and thighs and irregular areas of loss of all forms of sensibility on both sides of the abdomen up to the umbilicus; urinary retention with overflow dribbling and slight fecal incontinence. The reflexes and motor power of the upper extremities were normal. (There is no record of the motor power and of muscle tonus of the lower extremities.) Temperature on admission was 100 degrees Fahrenheit.

The examination of the blood and urine gave negative results. Lumbar puncture yielded a clear, colorless fluid under normal pressure, containing no cells and no globulin; the colloidal gold curve was: 133321111; the Wassermann reaction was negative in the blood and spinal fluid.

The patient was discharged from the hospital with the diagnosis of cerebrospinal syphilis on September 24, 1935 and was admitted to The Mount Sinai Hospital on the same day.

Examination. Here the examination on admission disclosed: a Horner's syndrome on the right side; slight rotatory nystagmus on looking to the extreme left; questionable weakness of the muscles of the right shoulder girdle; slight clumsiness of the left hand; paresis of the abdominal muscles with limited respiratory excursions and inability to sit up on account of weakness of the muscles of the back; spastic paralysis of both lower extremities, more marked on the left side. The tendon reflexes in the upper extremities were active and equal, except for the biceps reflex which was hyperactive on the left side; the suprapatellars could not be elicited; the right knee jerk was depressed and the left was active; the ankle jerks were depressed equally on both sides; the abdominal and cremasteric reflexes were absent; there were positive Babinski and Chaddock signs on both sides and a positive Oppenheim sign on the right. Sensation: Hypalgesia, hypthermesthesia and hypesthesia from the toes up to the fourth thoracic dermatome on both sides with a tendency to sacral sparing; the vibratory sense was diminished over the fourth, fifth, and sixth ribs below which it was absent, except over the sacrum and coccyx where it was diminished; loss of the sense of position in the toes of both feet. Occasional fibrillations were observed in the muscles of the lower extremities. The sphincter ani was relaxed. The heart and lungs showed no abnormalities. The liver and spleen were not enlarged and there were no palpable masses in the abdomen. There was no adenopathy. The vertebral column showed no deformities and there was no percussion tenderness over any of the bones.

Laboratory Data. Examination of the blood and urine gave negative results. Lumbar puncture (September 27, 1935) revealed complete subarachnoid block and yielded a clear, colorless fluid containing five lymphocytes per cu. mm.; the Pandy reaction was negative. The Wassermann reaction was negative in the blood and spinal fluid. Blood pressure was 110 systolic and 66 diastolic; temperature was normal. X-ray examination of the vertebral column gave negative results.

Course. On the day following admission the paralysis of the lower extremities became flaccid, the right knee jerk was more active than the left and neither ankle jerk was obtainable; there was a bilateral Babinski sign and complete loss of all forms of sensation from the toes up to the fifth thoracic dermatome on the right side and to the fourth thoracic dermatome on the left. Fecal and urinary incontinence persisted. Six days following admission lumbar puncture again revealed complete subarachnoid block and yielded slightly xanthochromic fluid. Lipiodol was then injected (by the cisternal route) and was found completely arrested at the level of the first thoracic vertebra (about the second thoracic segment of the cord).

On October 3, 1935, laminectomy was performed by Dr. Ira Cohen. The laminae

of the seventh and eighth cervical and of the first, second, and third thoracic vertebrae were removed and a granulomatous mass about 6 cm. long, 3 cm. wide, and 2 cm. thick, was found extradurally at the level indicated by the lipiodol, and removed. The pathologic tissue was also attached to the seventh cervical and first dorsal nerve roots on the right side and was somewhat adherent to the inner surface of the first thoracic vertebra. The main tumor mass was removed in one piece and the lateral extensions were removed piecemeal.

Following operation there was no recovery of motor or sensory functions of the affected parts, nor of sphincteric control. Within a few days there developed decubitus and ascending pyelonephritis with general sepsis; hypostatic pneumonia set in and death occurred from exhaustion on November 5, 1935, on the sixty-third day following the appearance of the first symptom of the disease.

Necropsy Findings. (A complete necropsy was performed but, for the sake of brevity, only the findings significant as far as this contribution is concerned are given.)

Gross Examination. The free border of the liver extended two fingers' breadth below the costal margin. The liver weighed 2410 grams.

The spleen extended one finger's breadth below the costal margin; it weighed 455 grams.

Spine. Section through the laminectomy wound disclosed no communication from the outside to the spinal canal. Upon separating the overlying tissues in this region a mass of granulomatous tissue was found on the dura at the level of the second and third thoracic vertebrae. Surrounding these two vertebrae there was edematous, firm, gelatinous tissue which did not, however, invade the bones. Anteriorly the prevertebral fascia over the bodies of the second and third thoracic vertebrae was thickened.

On longitudinal section of the second, third, fourth, fifth, and sixth thoracic vertebrae, the third was seen to differ markedly from the others; it was yellowish-gray in color; its trabeculations were indistinct and the body dense, compact, and sclerotic, but not altered in size or shape.

Lymph Nodes. On the left side of the trachea, about one-half inch below the larynx, there was seen a gland about the size of a walnut; it was firm, well circumscribed, and free from the surrounding connective tissue. On section, it presented many irregular grayish areas separated from each other by depressed darker areas.

The hilar nodes were enlarged, densely anthracotic, firm, and slightly edematous; on section, they presented many gray areas separated by depressed darker areas outlined by anthracotic pigment.

The inguinal nodes were also enlarged, discrete, and, on section, appeared similar to the other nodes. There were no other notably enlarged glands in the body.

Microscopic Examination. *Lymph nodes.* The nodes presented a varied appearance; in some areas the architecture was completely lost, whereas in others the structural characteristics were partially retained. The lymphatic tissue was replaced by a pleomorphic cellular tissue and by small areas of fibrosis. The cells consisted of many lymphocytes, plasma cells and large pale cells with large vesicular nuclei. Many giant cells, often multinucleated and vacuolated were observed (Fig. 1A). Fat stained frozen sections revealed fat globules in these cells. Atypical mitoses were frequently seen in the giant cells. Only rare eosinophiles were observed. The cells were present in varying mixtures in different portions of an affected node; sometimes the large pale cells predominated with only a slight admixture of lymphocytes and plasma cells. Capsular invasion was seen in foci. The fibroid areas stained well with the van Gieson stain and contained many lymphocytes.

Prevertebral Fascia. This fascia consisted of broad bands of connective tissue infiltrated by lymphocytes and occasional plasma cells. The attached muscle showed no abnormalities. In some areas of the fascia the infiltration consisted of dense collections of cells resembling those in the lymph nodes. The loose areolar tissue immediately beyond the connective tissue contained several nodular infiltrations resembling those in the lymph nodes.

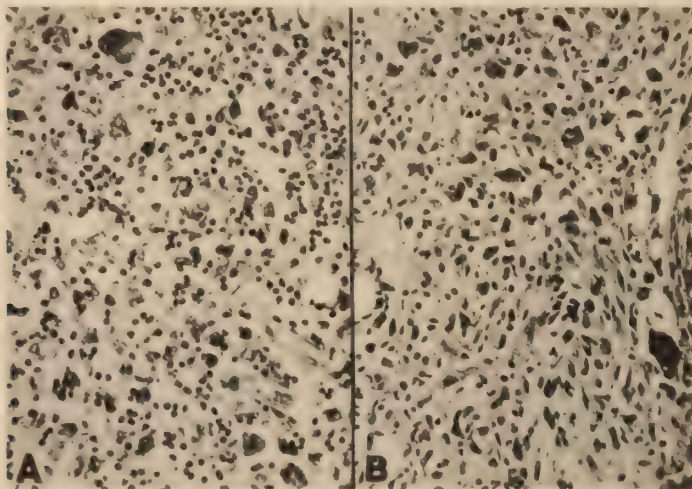


FIG. 1. Photomicrograph of (A) Lymph node typical of Hodgkin's disease. Note the giant cell in the left upper corner. (B) Bone marrow, showing cellular infiltration characteristic of Hodgkin's disease. Hematoxylin-eosin stain.

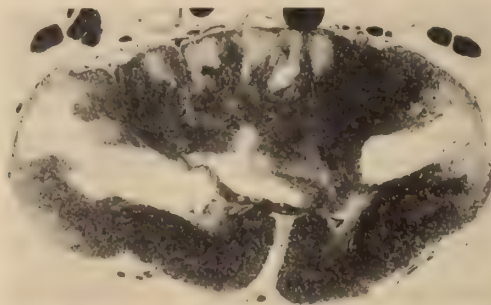


FIG. 2. Section of spinal cord through upper thoracic segment illustrating marked softening and disorganization of nerve tissue. Myelin sheath stain.

Tissue Around the Vertebrae. There was a varying degree of lymphocytic infiltration with occasional polymorphonuclear neutrophils and plasma cells. Areas characteristic of the picture described in the lymph nodes were not observed. There was much scarring of the striated muscle with the formation of new capillaries and evidences of destruction of adjacent bone.

Vertebrae. The third thoracic vertebra showed complete replacement of the marrow by osteoid tissue or very loose tissue consisting of spindle-shaped cells with ovoid nuclei and branching processes. Between these cells there was observed a

pale-staining homogeneous matrix which, for the most part, stained yellow with the van Gieson stain. Diffusely infiltrating this tissue were numerous lymphocytes, occasional plasma cells and histiocytes. In scattered areas there were seen foci of pleomorphic cellular structures resembling those in the lymph nodes. Osteoclasts was seen only in several small foci. The pathologic process stopped abruptly at the intervertebral disc and lateral margin of the vertebral body. The fourth

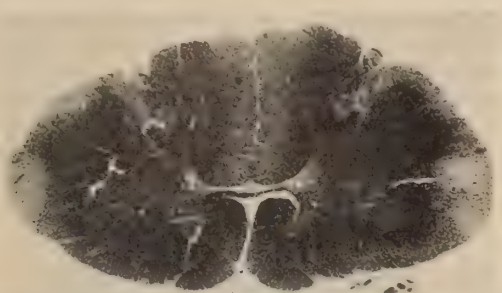


FIG. 3. Section through lower cervical spinal cord illustrating tract degeneration. Myelin sheath stain.



FIG. 4. Photomicrograph illustrating areas of complete demyelination, paling, granulation, and swelling of the nerve sheaths in the thoracic segment of spinal cord. Myelin sheath stain.

thoracic vertebra presented normal cellular marrow; in one area, however, just below the intervertebral disc, separating this vertebra from the one above it, there was found a nodule whose histologic structure was similar to that of the lymph nodes (Fig. 1B). No bone changes were observed in this vertebra.

The pathologic diagnosis was: Hodgkin's disease.

Gross Examination. Brain. Except for moderate cerebral arteriosclerosis and

slight opacity of the pia-arachnoid, particularly over the sulci, the brain showed no gross abnormalities. The scalp, calvarium and dura were normal.

Spinal Cord. On sectioning the cord, its segments from about the first thoracic to the seventh thoracic showed marked disorganization and softening (Fig. 2). This was most prominent about the fourth and fifth thoracic segments.

Microscopic Examination. A section of the cord in the upper thoracic segments disclosed an almost complete disruption and disintegration of the white matter. The tissue was spongy and fragmented. Myelin sheath stains showed large areas of complete demyelination (Fig. 3); other areas showed severe myelin changes consisting of paling, granulation and swelling of the sheaths (Fig. 4). Fat stains revealed a diffuse liberation of fat with dust-like granules thickly distributed. In addition to these, large numbers of gitter cells engorged with fat were scattered everywhere (Fig. 5). The changes in the gray matter were less severe, but the

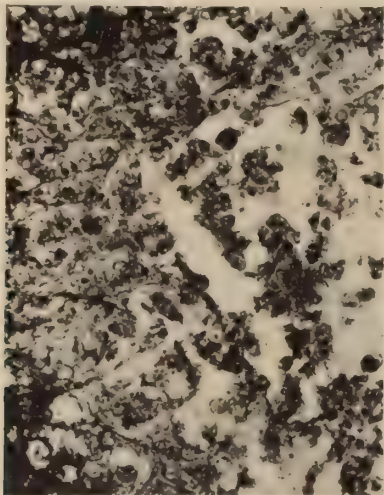


FIG. 5. Photomicrograph showing fatty degeneration of nerve tissue and gitter cells laden with fat granules.

ganglion cells showed large inclusions of fat surrounding the nucleus and displacing it in some cases. The microscopic diagnosis was: Myelomalacia.

SUMMARY

A previously healthy male, aged 49 years, while pushing a wheelbarrow full of coal over a plank, fell into an underlying excavation three feet deep with the coal falling upon his back. During the fall he bruised his right shoulder and abraded the right calf. He climbed out of the ditch unassisted and continued his work that day and during the next two days, following which there developed gradually a progressive weakness of the lower extremities so that sixteen days later he had almost complete motor and sensory paraplegia with vesical and rectal incontinence. The neurologic picture was that of an extra-medullary lesion compressing the spinal cord at a level approximately between the second and fourth thoracic segments. Manometric studies of the spinal fluid circulation revealed complete subarachnoid block. Lipiodol injected into the spinal canal was arrested at the first thoracic vertebra. A laminectomy was performed and a granulomatous tumor situated epidurally was found and removed. The tumor was 6 cm. long, 3 cm. wide, and 2 cm. thick and

extended from about the seventh cervical down to, and including, the third thoracic segment of the cord. Following operation there was no improvement in the patient's condition. Gradually there appeared cystitis, pyelonephritis, decubitus, general sepsis, bronchopneumonia, and the patient died sixty-three days after the onset of the first symptom of the disease.

Necropsy disclosed: 1) a recurrence of the granulomatous tissue over the dura at the site of operation; 2) a lymphogranulomatous gland to the left of the trachea and similar smaller hilar and inguinal glands; 3) a lymphogranuloma involving the entire third thoracic vertebra and a similar but smaller nodule in the body of the fourth thoracic vertebra; 4) lymphogranulomatous invasion of the prevertebral fascia overlying the second and third thoracic vertebra; 5) myelomalacia—a myelopathic process involving the upper thoracic segments of the cord, but most marked in the fourth and fifth segments.

COMMENT

The essential pathologic changes in Hodgkin's disease are in the nature of a granulomatous process of the lymph tissue and spleen. Although involvement of the lymph nodes, spleen and skeleton is most common, almost every tissue in the body may be affected. Predominating bone involvement, as in this case, in the presence of relatively slight involvement of the lymphatic structures is very unusual in Hodgkin's disease. Involvement of organs other than those of the lymphatic system may occur either by direct invasion of the pathologic process or by compression by adjacent granulomatous tissue. The symptomatology early in the disease is due to disturbances in function of the structures affected by the lymphogranuloma, whereas later it consists of a combination of these local manifestations and of symptoms referable to the effects of cachexia and anemia, or of a supervening infection.

Involvement of the nervous system occurs quite frequently. It is generally manifested by symptoms due to pressure by the granulomatous process on peripheral nerves or nerve trunks giving rise to paresthesiae, pains, vasomotor phenomena, and varying degrees of motor or sensory paralysis, or both; less frequently the neural symptoms may be those of involvement of the cord or brain and their coverings; in such cases the symptoms are produced by the pressure exerted upon these structures by the granulomatous tumor involving the spinal or intracranial dura, periosteum or bone. In most cases of Hodgkin's disease with involvement of the nervous system, neural manifestations appear late in the disease and are usually overshadowed by the symptoms of involvement of the glands, viscera and skin. This is especially true in most cases with involvement of the spinal cord. In the case reported, symptoms referable to spinal cord involvement were the first manifestations of the disease. As a matter of fact, the true nature of the disease was not suspected until the neurosurgeon had removed the tissues compressing the cord.

The most common forms of spinal cord involvement in Hodgkin's disease are: 1) Compression of the cord either by epidural or subdural deposits

of lymphogranulomatous tissue, or by involvement of one or several vertebrae with secondary angulation, producing the clinical picture of an extramedullary tumor of the spinal cord. 2) A myelopathy from circulatory interference in the cord by compression of the blood vessels of the cord by lymphogranulomatous tissue either within the intervertebral foramina, or outside of the spinal cord; in these cases the histologic picture resembles that of vascular myelopathy. 3) Changes in the cord due to a hypothetical toxin (?) of Hodgkin's disease which produces the histologic picture of subacute combined degeneration of the cord of the type observed in pernicious anemia, and in other anemias and cachexias. Two cases of Hodgkin's disease with the histologic picture of subacute combined degeneration of the cord have recently been reported by Shapiro (1). Weil (2), however, believes that the histologic picture in Shapiro's cases was not that of subacute combined degeneration of the cord of the type observed in pernicious anemia, but resembled that of a myelopathic process from interference with the blood supply and lymphatic circulation of the cord. This author collected forty-three cases from the literature and reported three personally observed cases of Hodgkin's disease with involvement of the spinal cord. In seventy-four per cent of these cases the thoracic segments of the cord were involved in the myelopathic process. The frequency of involvement of this portion of the cord is attributed by Weil to the fact that the blood supply in this region of the cord is taken over by the spinal branches of the intercostal arteries, and to the usual enlargement of the mediastinal and intrathoracic lymph nodes. From a study of these forty-six cases this author concludes that "involvement of the spinal cord begins at the end stage of a case of the disease that may have lasted from one to eight years." According to him, "signs of a complete spinal cord lesion develop rapidly after a short period of prodromal signs from one to six months before death and within a period of a few days or weeks at the maximum."

Trousseau divides the clinical course of Hodgkin's disease into two phases: 1) that of the beginning or local enlargement of the lymph nodes (latent period), and 2) that of the generalization of the process with involvement of the lymph glands generally, of the spleen in most cases, and of other organs and of progressive cachexia. Our case did not show the latent stage but conformed to the cases described by Arthur L. Bloomfield and others, in which the disease is first manifested by pressure symptoms, due to local involvement of vital parts (in our case, the spinal cord), and death occurs before generalization takes place.

From the operative and necropsy findings in our case it would seem that the lymphogranulomatous epidural deposits probably extended from the pathologic tissue in the affected vertebrae to the dura in the spinal canal. Many observers have reported that the lymphogranulomatous tissue reached the spinal canal by growing from the diseased mediastinal and

retroperitoneal lymphatic glands through the intervertebral foramina, in company with the nerve roots. In our case there was no demonstrable extension from the affected mediastinal gland to the spinal canal, and the nerve roots involved were the seventh cervical and first dorsal, both of which were remote from the affected vertebrae. The extension, therefore, was most likely a direct one from the diseased vertebra to the external surface of the dura whose resistance acted as a barrier to the invasion of the process subdurally. The epidural mass then acted as an extramedullary lesion compressing the spinal cord with resulting myelopathy from interference of the circulation in the spinal vessels. The histologic picture of the affected cord can be well correlated with this type of involvement of the neural structures, rather than with the type observed in the form of a system disease (subacute combined degeneration), which is due to some hypothetical toxin.

MEDICOLEGAL CONSIDERATIONS

Following the death of the patient, his heirs applied to the Workmen's Compensation Commission of this state for compensation. They based their legal claims on the theory that there was a causal relationship between the illness and death of the deceased and the trauma which he had sustained in the course of his occupation. By vote of four to one, the Industrial Board decided that no compensation was allowable because the death was not the result of the accidental injury.

The difficulty of determining the possible traumatic origin of cases of tumor, as well as of granulomatous lesions of the type encountered in Hodgkin's disease, is well recognized. "The chief task in determining the relation of trauma to any given tumor," says Ewing, "is one of laborious fact finding." By "fact finding", I take it, he means the determination as to whether or not a trauma has actually occurred; the nature of the trauma, and the site of the trauma in relation to the location of the tumor. In the case before us there is no question that the deceased was traumatized, but although the nature and severity of the trauma is known, there is a question as to the reasonable relationship between the site of the trauma and the location of the granuloma. According to the history, the patient scraped his right shoulder and right calf while he fell, and the coal fell on his back. Three areas were apparently traumatized but at only one of these (in the region of the third and fourth dorsal vertebrae) was there found a granuloma which produced symptoms during life. It must also be pointed out that, as far as could be determined, there was no external evidence of injury to any part of the back, although the earliest and most serious symptoms of the disease were those referable to the upper thoracic portion of the spinal cord.

The question now arises whether or not the injury to the back was sufficient to account for the pathologic process found at operation and necropsy.

Before this question can be answered with reasonable certainty, it must be determined, if possible: 1) whether the trauma was the exciting cause of the development of a granuloma in an individual who was predisposed to it; 2) whether the patient already had the tumor—the trauma, by its mechanical effect, enhancing the mobilization of the pathologic process; 3) whether the trauma was merely coincidental.

As long as the cause of Hodgkin's disease remains unknown, it is obviously impossible to express an opinion as to whether the trauma was the exciting cause of the development of a tumor in an individual predisposed to it. In this connection it must be borne in mind that there is abundant evidence that a single trauma of normal tissue is incapable of producing a tumor. According to Ewing, only those tumors may safely be referred to trauma in which the structure represents an exaggeration or variation of the normal healing process and its sequelae. In our case the histologic examination of the affected organs revealed no structural changes in the tissues which could be interpreted as an exaggeration or variation of the normal healing process.

As to the possibility that the trauma aggravated an already existing tumor, clinically the patient never presented evidences of the presence of a tumor prior to the trauma. Unfortunately the pathologist is unable to determine, with reasonable certainty, from the histologic appearance of the granulomatous tissue, its possible duration. In the present state of knowledge, therefore, there are no definite criteria that would enable one to determine whether the trauma aggravated a pre-existing tumor. By a process of exclusion, therefore, the physician would have to conclude that the trauma was most likely coincidental.

I am indebted to Drs. Paul Klemperer and Joseph H. Globus for the pathologic and neuropathologic data in the case.

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DETACHMENT OF THE RETINA: FACTORS INFLUENCING PROGNOSIS

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The modern operation for retinal detachment is now about ten years old. It has become possible to effect a surgical cure in a fair percentage of cases of what was formerly an incurable condition. In 1928, Gonin of Lausanne (1) pointed out the significance of rents or tears of the retina, which are almost always an accompaniment of the detachment. The main function of the operation is to seal off these tears, which apparently play an important, though ill-understood, part in the pathogenesis of the detachment. The operation, in addition, should evacuate the collection of subretinal fluid and allow the choroid to approximate the retina in a normal relationship. Finally, the particular technique employed should provoke a more or less localized inflammatory reaction which should make the choroid and retina firmly adherent.

The following two cases are reported as having certain distinctive features which made them unusually favorable for operation.

CASE REPORTS

Case 1 (Adm. 404760). S. M., a single woman, twenty-eight years of age, was admitted to the Eye Service in January, 1937 with an almost complete loss of vision of the right eye for one day. Her physician had diagnosed a retinal vascular block and the patient was immediately referred to the hospital for an anterior chamber paracentesis. More thorough examination revealed a retinal detachment of the right eye. The patient then recalled that she had struck the back of her head rather forcibly while straightening up under an open bureau drawer, two days prior to her loss of vision. There was a history of grippe and sinusitis a few months previously, but otherwise she had been in the best of health.

The patient's general physical examination, blood count, and urine analysis were entirely normal.

Ocular examination:—The right eye was the seat of a mixed astigmatic refractive error, as taken from the patient's glasses. (O.D.—1.00 sph. + 2.00 cyl. ax. 90°.) The vision in this eye was reduced to counting fingers at the distance of a few feet. The field was generally contracted, most of the limitation being above. The anterior portion of the eye appeared entirely normal, and the vitreous was clear and free from opacities. The lesion was entirely confined to the fundus. Almost the entire lower retina, extending up to the nerve-head and macula, was the seat of a flat detachment. This could be inspected at all places with a + 5.00 diopter lens in the ophthalmoscope, and there was no massive bulge forward. After thorough examination through a very widely dilated pupil, a small retinal tear was found in the extreme periphery

below, probably very close to, if not indeed at, the ora serrata (Fig. 1). The left eye was normal in all respects, the vision being 20/20 corrected by a + .50 cyl. ax. 90°.

Case 2 (Adm. 102516). L. G., a Mexican housewife, aged thirty-four years, was admitted to the Eye Service on December 19, 1936 for gradual loss of vision in the right eye over a period of thirty-six hours. A great many years previously there had been some difficulty with this eye, the exact nature of which she could not recall. There was no known injury prior to the immediate visual loss, and, apart from slight nausea (which she ascribed to worry), she had felt well.

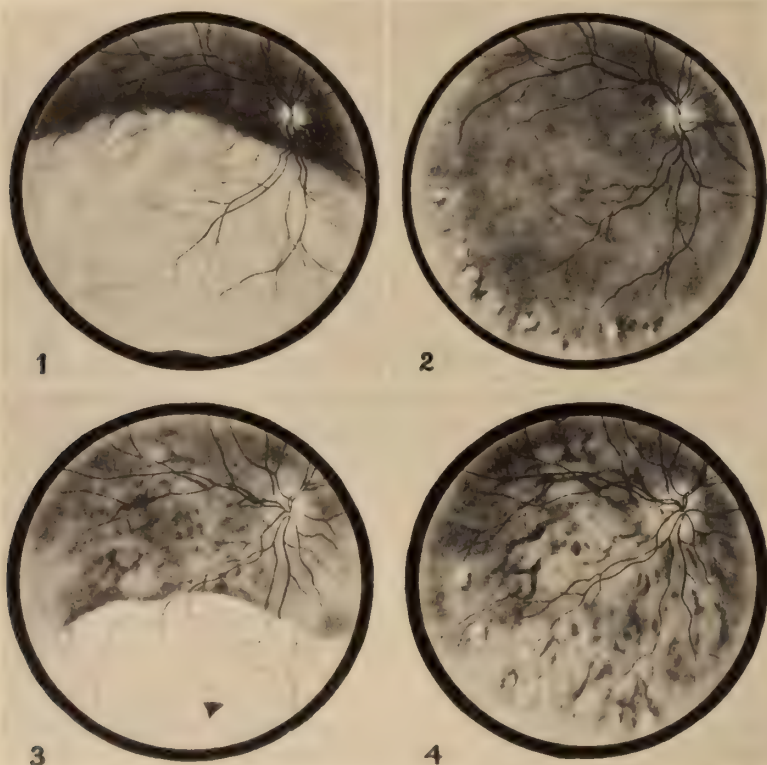


FIG. 1. Case 1, S. M., before operation, showing tear

FIG. 2. Case 1, S. M., after operation

FIG. 3. Case 2, L. G., before operation, showing tear

FIG. 4. Case 2, L. G., after operation

The general physical examination, blood count and urine analysis were normal.

Ocular examination showed vision in the right eye to be reduced to hand movements in the lower field. No accurate field-plotting could be undertaken. Anteriorly the eye appeared normal. There were many fine dust-like and stringy vitreous opacities which somewhat obscured the view of the fundus. The fundus itself showed the changes of very high myopia, the nerve-head being seen best with a -25. lens. The infero-temporal retina bulged forward into the vitreous in the form of a bulbous detachment, and at 5:30 o'clock, some distance from the ora serrata, there was a triangular tear with its apex directed downward (Fig. 3).

O.S.—The corrected vision of this eye was 20/70 and apart from a high myopia, the eye was normal.

OPERATIVE TECHNIQUE

The same technique was followed in operating the two foregoing cases.

The eye was anesthetized by a subconjunctival injection of novocaine. No drops were instilled in order not to cloud the cornea, and retrobulbar injection was also eliminated in order to avoid hypotony of the globe. A small marking suture was placed at the corneal limbus in the meridian of the tear, and an incision of the conjunctiva was made over the region of the tear, 15 mm. from the limbus. The conjunctivae and Tenon's capsule were dissected away from the sclera, and the external and inferior rectus muscles were mobilized. Heavy sutures were then passed around these muscles, which were used to retract and to rotate the globe into position. The site of the tear was approximated by measurement from the limbus, in the direction of the marking suture, and a Safar needle was inserted at this point, penetrating the coats of the eye with high frequency current. The fundus was then observed and the relation between the tear and the coagulated area on the retina noted. The properly oriented tear was then surrounded by a row of needle punctures, and a second row of small areas of surface coagulation was made with a ball electrode beyond these. The sclera was then trephined at the most dependent portion of the detached area, the choroid punctured, and the subretinal fluid was allowed to escape. Tenon's capsule and the conjunctiva were then sutured, and a binocular dressing applied.

DISCUSSION

Operative reattachment of the retina was obtained in these two patients; this has persisted to the present time. It will be noted that the cases had several features in common. Both patients were young, in good general health, and, apart from the detachments and high myopia in the second patient, their ocular status was normal. Locally, the retinal tears were single and inferiorly placed. In both instances the patients were seen and operated upon within a short time after the onset of the detachment.

Of course, no specific inferences can be drawn from separate case reports of a condition as protean in its nature as retinal detachment. They do, however, emphasize the fact that, given favorable conditions, a good operative result may be anticipated with some degree of assurance. In the present state of our knowledge a guarded prognosis is practically always given in retinal detachment. As the influencing factors crystallize out with greater clarity, there is less reluctance in separating cases for operative treatment from those in which surgery would be meddlesome, if not dangerous.

The question of the permanence of reattachment must also be con-

sidered. Arruga (2), who recently published a comprehensive study of three hundred cases, states, "The frequency of recurrences and relapses diminishes with the lapse of time after the operation. If two months have elapsed during the latter of which the patient has carried on a normal life, the chances of permanent cure are good, although of course, never certain."

The two general factors influencing prognosis in retinal detachment are, as in all surgical procedures, the age of the patient and the state of general health. The local factors are undoubtedly not all known at the present time. Some of those which can be enumerated are: 1. The mechanism of the detachment, the traumatic variety responding better than where the element of inflammation, high myopia, or retinal degeneration is present. 2. The length of time the detachment has been present. 3. The absence of any bands or organized connective tissue holding the retina away from the choroid. 4. The position and nature of the tear. Single tears, inferiorly placed, seem to have the most favorable prognostic significance.

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PSYCHOTHERAPY IN MENTAL HEALTH CLINICS

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In a paper published in 1924¹ Freud remarks that: "At present we can do nothing in the crowded ranks of the people who suffer exceedingly from neuroses . . . at some time or other the conscience of the community will awake and admonish it that the poor man has just as much right to help for his mind as he now has to the surgeon's means of saving life; and that the neuroses menace the health of a people no less than tuberculosis, and can be left as little to the feeble handling of individuals. Then clinic and consultation-departments will be built, to which analytically trained physicians will be appointed, so that the men who would otherwise give way to drink, the women who have nearly succumbed under their burden of privations, the children for whom there is no choice but running wild or neurosis, may be made by analysis able to resist and able to do something in the world. This treatment will be free. It may be a long time before the State regards this as an urgent duty. Present conditions may delay its arrival even longer. . .

"The task will then arise for us to adapt our technique to the new conditions. I have no doubt that the validity of our psychological assumptions will impress the uneducated too, but we shall need to find the simplest and most natural expression for our theoretical doctrines. We shall probably discover that the poor are even less ready to part with their neuroses than the rich, because the hard life that awaits them when they recover has no attraction and illness in them gives them more claim to the help of others. . . It is very probable too, that the application of our therapy to numbers will compel us to alloy the pure gold of analysis plentifully with the copper of indirect suggestion; and even hypnotic influence might find a place in it again, as it has in the treatment of war-neuroses. But whatever form this psychotherapy for the people may take, whatever the elements out of which it is compounded, its most effective and most important ingredients will assuredly remain those borrowed from strict psychoanalysis which serves no ulterior purpose."

The acuteness of these observations is demonstrated in the ever-increasing extent to which hospitals nowadays find it necessary to open their out-patient departments to patients suffering from nervous disorders.

¹ Freud, Sigmund: *Collected Papers*, Vol. 2, page 401. Hogarth Press, London, 1924.

The medical world in general is more open-minded to the understanding of nervous disorders and their causation, an understanding to which the psychoanalytic concepts have added greatly. In fact, they have enabled us not only to explore many mental disorders previously considered unapproachable, but also to rehabilitate the neurotic more fundamentally than had previously been deemed possible.

Not so long ago, when psychotherapy was practiced as a part of general medical therapy, neither patient nor physician had any clear comprehension of the methods employed. Limited to attempts at re-education by suggestion, persuasion, appeals to the patient's logic and reason, these methods obviously constituted a superficial approach. They overlooked those most important emotional factors which dominate present-day psychotherapy.

Our present-day approach is on a quite different basis. True, we employ the same methods, but now the physician has acquired some knowledge, however limited, of the conflicts which may have acted to bring about and maintain the patient's current symptoms. It is certain that the neurotic himself does not understand his sufferings. He is aware only of the symptoms that they cause; the motivations of those symptoms are unconscious. In a way, this unawareness is a means of self-defense. For he would not be able to accept and face consciously all his infantile anti-social strivings, were he aware of them. He would not be able to realize or accept his own shortcomings, and understand all their ramifications. There are feelings within him that he does not dare to recognize or respond to in even a slight degree. This means, for example, that his shortcomings may make him feel inferior in his surroundings. Perhaps as an office worker he is too often made to feel his inferiority by fellow workers or superiors. In consequence he may develop strong feelings of aggression which, however, instead of realizing, he internalizes, chokes up within himself, until on this basis he develops neurotic symptoms.

Joining this over-aggressiveness, which is such a significant constituent of the neurotic conflict, are still other unconscious forces, even more difficult for an individual to accept as part of himself. These are distortions in the love-life, always closely connected with early environment (the family), and the concomitant sexual difficulties from which the neurotic may suffer.

To alleviate or modify these symptoms, the first step necessary is to acquire an understanding of the patient's personality and his mode of reacting in society. Similarly it will be essential to recognize the earlier patterns which, during his childhood and youth, became the foundations for his later form of reaction.

Our aim, then, is to teach such a patient to understand himself and his psychic motives better, to learn to accept his own faults and not to punish

or abuse himself for them, as well as to recognize his potentialities, to appreciate his own (even if limited) abilities, and to utilize them for his own good. In psychoanalytic terms, we wish to make his *superego* (conscience) more lenient towards his own faults and limitations, his so-called "inferiorities." The patient must be brought to realize that the demands he makes upon himself are too severe for him to cope with and he must be satisfied with their fulfillment in a lesser degree.

We must bear in mind the fact that the patient's present conflicts and reactions are linked up with the deep past, and the environment which causes the patient to react as he does at present is to some extent a replica of the environment of early childhood. At that time it consisted of the parents and siblings; now it consists of members of society, representing, as they do in the unconscious, brothers and sisters, or even fathers and mothers.

The early environment created a strong tie of love between the infant and the parents, particularly the mother, who became the first object of the child's love. But although there was at first only love, after a little while anxiety arose, the result of frustrations. Parallel with anxiety, aggression developed against those persons who thwarted the weak child in the realization of his desires. A child must learn very early in his life to deal with the basic emotions of love, fear, and aggression.

Out of all these feelings he eventually develops a social *superego*, in reality the incorporated image of the parents. Part of this *superego's* function is to threaten the child into good behavior and obedience, thus directing him towards social adjustment. The other part of its function will be to serve as a love-object, as an example of the person the child would like to resemble.

The growing child perceives the nature of reality with increasing clearness. He experiences and learns to live up to its demands. At the same time he learns to differentiate between the kindness of the external world and the cruelty and mercilessness with which that same external world demands the enforcement of certain of its laws. This arouses in him a hostile feeling against his environment. Thus what we later learn to recognize as ambivalence of feeling—love and hate for the same object—an emotion responsible in adult life for neurotic difficulties, is present in the growing child. The early patterns of development are shaped by an environment which both loves and chastens.

In its turn the child accepts these patterns partly because of love and partly because of fear. The strength of the emotional tie between child, parents, and siblings, which exists in the early environment, may result in a permanent over-attachment, which, carried over into later life, may bring about a condition in which the person cannot get along independently but must always have someone to lean upon. At the same time the

amount of hostility with which the child reacts to early environmental frustrations may result in an over-aggressive reaction to all frustration which may then color his attitude throughout life.

The neurotic person is too much like a child in his desires: not satisfied with partial realization of them he demands the whole, and all of it at once. Thwarted, he grows impatient, disappointed, fretful, ready to accuse the whole world of lack of understanding and sympathy with him.

Yet when we survey the origins of personality structure in childhood, always keeping in mind the fact that the child's adjustment is due to his obedience out of either love or fear, it becomes clear that the neurotic symptoms of later life express some particular aim of the afflicted person.

Let us, for instance, examine neurotic anxiety itself. At once we can see how it serves the purpose of getting affection and sympathy for the sick person. At the same time, however, we can also conceive that self-punishing tendencies find their expression in this symptom. The conflict is always between those tendencies and strivings which may be described as being of the *id* (unconscious) part of the personality, and of the *ego* (conscious) part of the personality. Here the *ego* may also denote cultural demands and social adjustments. In the neurotic the *id* tendencies are very vigorous, preserving within them remnants of childhood emotions. For this reason the *ego* has the harder task in keeping them back from realization. The conflict between the conscious and the unconscious tendencies may reveal itself in a variety of symptoms.

To further the therapy, which ultimately tends to socialize the patient's emotions and readjust him in society, it is of prime importance to have good contact with the patient, to bring about a successful "transference." In this way the patient is made to appreciate the distinction between those of his fears which are real and those which are imaginary (and neurotic fears are more often imaginary). When the patient has learned to understand his fears and to be ashamed of them, he sees how he has been inhibited by such (nonsensical) fears. To reduce fear reactions we must work intensively on the emotion that accompanies fear: aggression. Once the patient understands his anxieties, he perceives that they are closely connected with his repressed aggressive tendencies and serve as a defence against the breaking through of those aggressions. Being afraid of "going crazy," for example, is really a defence against letting go and actually doing something irresponsible—crazy.

The following case history will illustrate some of the points theoretically considered above.

A man in his twenties, married and the father of a child, presented these symptoms: pressure on the top of the head, accompanied by dizziness; slight confusion at times; severe anxiety spells during which he perspired profusely, trembled and cried, without being able to give any reason, and after which he had to lie down to rest because he felt weak and helpless. His condition was diagnosed as anxiety

hysteria; although the question of organicity, the possibility of the attacks being epileptic in nature, was also considered.

Closer investigation revealed that the anxiety spells had a content, to wit, that the patient was afraid of going crazy. These fears were evoked by the sensation of pressure on the head. In addition he had a secret terror of death. At this point the question was inevitable: what could cause such thoughts and fears in the patient's mind? To understand his symptoms, in fact his entire illness, the whole background of his life had to be investigated.

The patient held a unique position in his family, being employed by a relative and also called upon by all the members of the family for all kinds of auxiliary work. For this he felt himself to be inadequately compensated materially, particularly in comparison with what the employing relative received. However, his responsibility to his wife and child and the difficulty of breaking away from his family made him cling to the detested job.

This situation had been going on for years, growing worse instead of better. He had to use increasing compulsion on himself to live up to the demands of his employer. On the one hand he would have liked to strike out on his own, to make himself independent; but on the other, he was afraid that in view of the difficult economic situation he would not be able to find any security, and in the meantime he had a wife and child to care for. He felt that if only he were alone, independent, not burdened with a wife and child, he would be able to do it. But as it was he felt himself forced to stick to his job.

His exasperations accumulated with the years. He grew to detest his job more and more, revolted against it, and even brought himself to the point of demanding a raise in salary. But even after he got this he was still fundamentally unsatisfied. He lost weight constantly, complained of feeling tired and weak, of all sorts of pains, and was then sent to the hospital by his family.

After the question of organic illness had been excluded, the psychotherapeutic process continued along these lines: winning the patient's confidence, inducing him to tell as much as he wishes of his intimate life, of his relationship with his employer and family. He may not yet be aware how great the resentment is that he feels against them. He feels only the resentment, not the connection between it and his anxiety symptoms, such as his fears of going crazy. Behind this fear, which is closely connected with his confusion, lies an unconscious desire to do some (crazy) thing, to act irresponsibly, if only for a little while, to carry out certain cravings such as telling them all "where to get off," or even beating up his boss. The others would certainly consider these desires "crazy" if they had an inkling of them. The anxiety he has developed acts to curb these secret wishes by keeping him so busy with fears as to divert his attention from open revolt.

As this patient has a strong tendency to be dependent and rely on someone else, the therapeutic process will set to work employing this tendency. The therapist will permit the patient to rely upon him for advice and sympathy—transference. With the help of this transference the therapist should be able to assist the patient to perceive the relationship between his emotions and his actions. He will be made to understand that under the circumstances his resentment may have been justified; that the unconscious guilt he feels as a result of the aggressive ill wishes

against his family is also natural, arising from the instinctive side of his personality.

In other words, he must learn to understand that his primitive selfishness revolted, wanting to get even, perhaps by desiring to attack someone or wishing his death. Now the patient's conscious, logical, cultured ego has tried to dismiss and repress such "ungodly" thoughts (for he is a religious man) which make him feel guilty. And so his inner life has become an unceasing conflict.

The variety of neuroses and personality maladjustments is great and in clinical treatment there are as many therapeutic approaches and processes as there are types of neuroses. The patients with whom we deal in this clinic are, to be sure, extremely varied; yet in the final analysis the illness is always due to actual causes and childhood pathogenesis.

The best cases for psychotherapy in the clinic prove to be those which we know under the collective name of transference neuroses or conversion hysterias, according to the predominance of the symptoms. If the hysterical condition predominates, the case is typed as a conversion hysteria; if the anxiety is outstanding, we consider it an anxiety neurosis.

Another frequent type encountered in the clinic is the compulsion neurosis. We also meet the character neurosis, or types of neurotic character, which are difficult to deal with because they are asymptomatic; without showing actual illness, their total personality, the actions of their daily life are permeated with asocial characteristics. They may also be classified as problems of behavior.

When first observed, all these patients are at odds with their immediate environment. Their adjustment to this environment is our main task. Nevertheless, we always know that there does exist, deep within them, the prototype for these environmental difficulties, and that the difficulty is with the childhood relationships to parents and siblings in the home.

Results of varying degrees will be obtainable even if the treatment be somewhat superficial when compared with the psychoanalytic treatment in the office, for the personality structure of these patients is strong enough to stand considerable abuse and pressure from without. True, they are inhibited and repressed, but to ease even slightly their repressions and inhibitions may make them more tolerant. Then, too, the ability to ease these repressive and inhibitory tendencies implies an ability on the patient's part to tolerate more and prepares the way for liberating, for social purposes, the energies formerly used by the patient to keep constant check on himself.

These patients have a certain insight into their difficulties, although they may be blinded by overmuch subjectivity and emotional entanglements. If the latter are clarified, their insight into their difficulties improves and helps them to understand the origin and "aim" of their symptoms. It becomes clearer to them how and why the symptoms made

them helpless and crippled. They see that their inhibition is closely connected with excessive self-criticism, which they presently learn to moderate.

Even for patients with psychotic trends, who have maintained some degree of their healthy personality structure and are only partly disintegrated, a great deal can be done to keep them out of institutions. To illustrate the importance of the method of approach and the necessity of individualizing it to conform with the patient's illness, I shall cite the case of one patient of this type.

This patient had definite paranoid delusions, a fundamental distrust of any form of medical therapy, and an excessive hostility towards receiving help. He attributed hostility to everyone, even to the physicians. I saw him as a "private" patient. He was brought to my office by a social worker from one of the agencies, because he had steadfastly refused to go to any clinics, and the agency, interested in his family, did not want the responsibility of committing him to a state hospital when neither he nor his family would consent to a commitment, despite his mental illness.

In my interview with him I succeeded in getting him to go to the Physiotherapy Clinic for the electrical treatments which he thought might help him, although the doctors did not think so. He complained of all sorts of aches and pains: pains and pressure in the head; rush of blood to the head with a consequent fear of hemorrhage; pains in the genitals, which he attributed to the sexual relationships with his wife, to which he forced himself in order to satisfy her.

His paranoid ideas at the time concerned his belief that his neighbors and fellow workers wanted to harm him. He admitted that there was no reason for thinking this, but he could not help his feelings. He was over-conscientious, and could not bear the thought of dishonesty. His speech was frequently incoherent, rhapsodic and disconnected, the sentences left incomplete.

He was in the late twenties when I first saw him. He followed my advice and went to the Physiotherapy Clinic. I had told him that I was on the same floor, in another clinic, and whenever he wanted to he could come in and tell me how his electrical treatments were getting along. In this way I hoped to get his confidence and effect a transference relationship to the Mental Health Clinic—which did happen. For a number of weeks he went to the Physiotherapy Clinic, where the physician-in-charge was ready to cooperate by giving him treatments for suggestive purposes; one day he spontaneously walked into the Mental Health Clinic. We talked a little and I encouraged him to continue the treatments he was taking, which he did; eventually, after many weeks, he came over to the Mental Health Clinic, ceasing to attend the other clinic.

At present he has been in the care of the Mental Health Clinic for more than three years. Compared to his condition when I first saw him, he has made a remarkable if partial, recovery. I wish to emphasize this fact, for throughout the period of his treatment we had many conferences about him and were more than once ready to commit him. However, he managed to pull through and has thus far escaped that fate.

In the course of his visits to the clinic the following history was obtained:

He was born in Russia, the third of four children and, according to his report, the parents' favorite. However, he was always more attached to his mother, an aggressive woman who helped out his father by conducting a business of her own until she had a nervous breakdown. The patient had a faint suspicion that there was some connection between his illness and his mother's nervousness, although

he disliked mention of it. It was really the mother who brought up the children and she reared them very strictly, particularly with regard to sexual matters. Incidentally, it was she who gave the patient his enlightenment about sex. In his opinion the parents' marriage was unhappy.

During the course of the treatment he often contrasted himself with his father, who was a handsome, well-groomed, self-centered man. The patient claimed to have been friendly with people in his youth. While still in his teens he had to go to work to help his father in business. He came to the United States to escape conscription into the army.

When he first arrived in this country he went to live with an aunt, whom he blames for his nervousness, saying that she was like an evil witch to him. Among other things, she induced him to change his name, which he now regrets. He worked steadily at his trade and made a good salary. He soon married a woman who was good looking and whom he considered superior to himself because of her command of English which he did not have, but after the marriage he discovered that she was ignorant and much inferior to him. He often used to point out to her the superiority of his family to hers.

Shortly after the marriage he began to suspect his wife of infidelity; when he heard his fellow workers boast of their affairs with women, he could feel the blood rush to his head, and he would be compelled to think of his wife: where she might be and what she might be doing. He went so far as to leave the factory early to see what she was doing. At that time he became so depressed that he contemplated suicide, but did not carry out his plan because of his interest in his children. While he was in this depressed state he had to go on relief. In fact, when he came to the clinic, he had already been on relief two years and his wife had begun to go out to do housework.

After he had been coming to the clinic for more than a year it was revealed that his suspicion of his wife and his pathological jealousy had their actual roots in his wife's confession, just before their marriage, that she had had a premarital relationship at the age of sixteen. He was deeply shocked to hear this and married her only because she threatened suicide if he did not. Although he never forgave her, still it is interesting to note that he tried to have sexual relationships with her quite often in order—as the treatment brought out—to prove his superiority to her, to satisfy her, and to enjoy vicariously her gratification, thus making her love him.

It was tremendously important to this patient to be loved by everyone. His paranoid ideas that people were persecuting and wishing to harm him were really the reverse of this wish to be loved. He had the feeling that he was not loved enough; much like a child's feeling about love, which does not admit of indifference. The child knows only two extremes: either people show affection and attention, proving that they love him, or by not showing affection, prove that they do not love him. Indifference, to the child, is equivalent to not wanting him, resenting him, and rejecting him. For this patient the situation was psychologically the same.

It took long months of treatment before he began to relax, become confidential, and discuss more than his perpetual complaints, fears and paranoid ideas: to talk candidly about his life. Then, as time went on and he became less distrustful, his fears gradually began to give way to resentment and aggression—the reverse of his primary fear that people were angry at him and wanted to do him harm. It became obvious, as we had suspected from the start, that he was full of rage and aggressiveness, that the fears were merely a reversal of, and a defense against, his own aggression and hostility. In about a year and a half he advanced so far that although he still had paranoid ideas, he was more composed and able to make social contacts. And where he had at first talked only about his concern for his wife and children,

he now found himself able to talk about his resentment against his wife for her premarital affair.

All this time we were trying to keep him and his complaints on a reality basis, always laying stress on those complaints that had to do with actual situations in his work, his contacts with people, his family, and his wife. His relations to his parents had also become the object of many discussions, accompanied by emotional scenes. He had brought both parents over to this country but, as his mother did not get along well with his father, she went back, while the father stayed on with him and his brother. This saddened and embittered him because he felt that when he had had money everyone relied on him and now that he had none, he had no one at all to confide in or rely upon.

His need for reliance which the clinic satisfied, and his "transference" relationship to the therapist furthered his improvement. He was given the opportunity not only to express his need for someone to care for him and be interested in his problems, but also to see and then to express his resentment against and disappointment in the frustrations by his wife, his family, and society. He was guided to form new emotional reactions and ties in his social relationships. Little by little the psychotic phenomena disappeared and he acquired new insight into his former psychotic phases. His various bodily sensations diminished and finally ceased. At the present time he is looking for a job; instead of being interested exclusively in his own sensations, his interests have turned objectively toward his family, society, and work.

An important task in the therapy was to make the patient more tolerant towards himself, once he had gained insight into the structure of his conflicts. This task, incidentally, is one that confronts us in dealing with nearly every neurotic. The neurotic must be brought to realize that the demands he makes upon himself are too severe for him to cope with. To bring about a readjustment in the patient's emotions, to make him more socialized, the necessity of a good contact with the patient can not be over-emphasized. This contact is what we term "transference." It is emotionally based on the mutual dependence of all human beings; its prototype is the child's dependence on the parents.

In the neurotic this desire for dependence, for some emotional tie, is very strong, and once grasped, it can be utilized in psychotherapy. As the names positive and negative transference indicate, the concept includes both emotional poles, love and hate. And although the effect of the positive transference was realized and employed in all psychotherapies before analysis, only in the course of psychoanalysis have we come to recognize fully the importance of both of these phases of the emotional relationship.

Investigations of the personality structure of neurotic persons have taught us that their great difficulty is the retention in adult life of too many childhood strivings. At the same time their emotional life is also child-like in type. Their love and their desire to be loved are present to a degree greater than is common. Their anxiety and fear of being left on their own, to face or combat reality, are also hypertrophied. Since they

are unable to respond at an adult level to the daily demands of reality, the tendency to run away (regress) will bulk large in their lives.

Consequently we cannot avoid the presence in these patients of negative feelings, feelings against the clinic, the therapy, or the physician. It is just as important for the patient to recognize these feelings as it is for him to recognize and express his negative, antagonistic feelings against society or the members of his family with whom his neurosis may be connected. It is difficult to deal with the patient's negative attitude towards the physician or clinic because he may feel that as a "charity patient" he is not free to criticize. Nevertheless, to some slight degree at least, his criticisms must be encouraged.

Plainly this cannot be done to the extent possible in private practice. For in the clinic, what we must treat are the acute problems and the current emotional entanglements of the patient. Of course, we must discover the events which preceded and precipitated the patient's actual neurotic reaction, but in the clinic interviews, which are limited and not resumed daily, it is inadvisable to delve into the deeper unconscious material.

PSYCHASTHENIA

A CLINICAL AND PSYCHOPATHOLOGICAL ANALYSIS*

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In the present communication I wish to report the results of an analytic study of the symptomatology, manner of development and effects of treatment in a series of cases clinically diagnosed psychasthenia. The series comprises twenty-eight patients (eighteen female and ten male) who were admitted to the hospital during a five year period beginning in 1930. In age they ranged from 13 to 46 years, in intelligence quotients from 63 to 122, and in their social and financial status, the localities from which they came, training and racial stock, they represented an adequate random sample of the general population of the state. They were not selected cases, but comprised all of the definitely diagnosed psychasthenics that were admitted during this period; and when we consider the fact that the total first admissions to this hospital for the five years consisted of 1,500 patients, it might very well be asked whether a study of a disease that is so meagerly represented could be considered of general importance in neuro-psychiatry. At the outset, therefore, I should like to emphasize the fact that the problem involved here and to be discussed in this communication is of far greater importance than the numerical proportion of the patients studied. As one considers the question of differentiation within the field of psychiatry, it becomes clear that there are very few, if any, nosological entities in which the question I wish to raise with regard to psychasthenia has not come up at one time or another. This question might be stated somewhat as follows: In grouping any given number of cases under the concept of a special diagnosis, do we deal with a real disease entity; and what are the theoretical reasons for, and practical advantages that we derive from, such a diagnosis?

In regard to psychasthenia, this question is neither new nor recent. In fact, it would seem that ever since Janet first used this name (in 1898) and described its symptomatology (in 1903), a great many workers in this field have now and again raised the question of the justification and advisability of segregating all these clinical pictures under the heading of one term. The dilemma with which we are faced is that the term has persisted in spite of the objections raised against it. At present it is still

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officially being used in the psychiatric nomenclature, which would indicate that all of the cases diagnosed psychasthenia must have some important common features. On the other hand, the fact that serious and able investigators have raised objections to the inclusion of all these, rather heterogeneous, pictures under the same diagnosis, would indicate that there are fundamental differences between these cases. The literature on this subject and the controversies between the advocates and the opponents of the concept is so large and at the same time so well known, that there is little necessity for reviewing it here. Some authorities have shown very pronounced differences in the clinical pictures on the basis of phenomenological analysis (Schneider). Others brought out differences of dynamics and etiological features (psychoanalysts). Still others have shown divergences in prognosis, methods of treatment, relationship to other diagnostic entities, etc.

In the present discussion I should like to stress particularly the practical aspect of the problem. Here we have a series of maladjusted persons, all of whom present symptom complexes, which were nosologically classified by the staff of this hospital, and would be so classified by other psychiatrists as belonging to the group of the psychasthenias. All of these cases were investigated clinically and treated for periods of time ranging from several weeks to several months. Thus we have had an opportunity to study the types of personality, the development of the symptoms and the effects in one way or another of the various attempts at treatment. To complete the analysis, we have undertaken a study of the adjustment of these people after they were discharged from the hospital, and all of the cases have been followed for periods varying from three to seven years. The question at present therefore is as follows: Is it practically useful and theoretically justifiable to consider all of these problems as involving some fundamental function and can we, on the basis of this, establish a uniform type of treatment and predict more or less similar prognoses, or are the main differences so great that it will be more advisable to look upon this series as divisible into several groups that differ in all these respects? It is for this purpose that I have attempted an analysis of the material in relation to three fundamental factors:

1. The clinicopsychological picture.
2. The etiology.
3. The treatment and its results.

As a starting point in this analysis let us discuss those clinical manifestations which Janet himself and most psychiatrists following him have considered as belonging to this group and see what the fundamental psychological feature is which characterizes all of them. The symptoms most frequently spoken of as belonging to psychasthenia are phobias, obsessions, compulsive acts, states of doubt and hesitation, and certain types of morbid anxiety. As a fundamental characteristic of all of these,

we usually think of a feature which is probably best described by the German word "Zwang," and for which I can find no adequate translation in English. Recently Schneider, in his discussion of the psychological features of these symptoms, suggested that the word "Zwang," since it did not permit the formation of an adjective, was not quite suitable for the description of the personality characteristics involved and has proposed that it be replaced by the word *anankastic* which, since it comes from the Greek, could just as easily be used in English as it is in the German literature. Essentially anankastic symptoms, whether they be ideas, manners of thinking, feeling, or response have this in common: that they take place within the person, but apparently outside of the scope, and even in spite of that component of the personality that may be described as the "Ego." By the Ego, in this respect we mean the conscious, volitional, logically controlled component of the personality. The psychasthenic who feels forced to hesitate and to doubt in the performance of all his activities, the one who is obsessed by painful thoughts or phobias or, finally, the one who must continually wash his hands, all have in common the characteristic that they feel "compelled" to carry out these phenomena, although logically they can see no reasons for them.

The next step in our analytic approach would be to ascertain a) whether all anankastic phenomena have a fundamental psychiatric uniformity; and b) whether they should be regarded as occurring exclusively in psychasthenia. The second part of the question must be answered in the negative, because we know that symptoms of this type are not at all restricted, even to that broad field which is covered by the psychasthenias. On the one hand we find them in other diseases, such as depression and schizophrenia, and recently they have been reported even in organic diseases such as the post-encephalitic syndromes. On the other hand we frequently find them in certain types of personality anomalies and, in a rudimentary state, even in the everyday life of the average individual. To this one might retort with the argument that in all of the other conditions mentioned, the anankastic activities are neither primary nor fundamental but must be regarded as accessories and of secondary development, whereas in psychasthenia they are the central characteristic feature. The first part of the question, namely the one concerning the psychiatric uniformity of these symptoms must also be answered in the negative, since a careful study of the material shows such wide divergence, that fundamentally the whole syndrome seems to fall into several distinct groups. It is of particular practical interest that these divergences are not restricted to the clinical pictures but seem to be definitely related to the etiology and the treatment indicated. Since it is impossible to report adequately the analyses of all the cases in this space and all of them seem to fall into distinct groups, I propose to present in the following three case analyses the distinctive features of the main groups.

Case 1. F. M. C. A 34 year old married woman was brought to the hospital because she had been expressing peculiar fears and had been behaving in a manner which was different from her usual way before the onset of the illness. The history of the present illness dated back about eight years, when the patient was pregnant with her third child, but the symptoms became especially pronounced during the last year when they began to interfere seriously with her adjustment. This exaggeration of the symptoms seemed to have started when the patient received a phonograph as a present from her aunt, and although she had been known to like music, refused to allow this phonograph to be played, without being able to give any reason for it. Following that she began to develop various fears, such as being afraid of the occurrence of a fire in the house; she would often forbid the building of a fire in the stove, actually pouring water on it if it was started. Then she began to be afraid of eating food prepared in the house, and refused to allow others to eat it. On some occasions she poured kerosene on the food so as to prevent its being eaten. She began to express fears of putting on her clothes or taking them off, of going to bed at night or starting any type of new work, because, she said, "something terrible would happen" if this were started. Another distressing symptom was her constant hesitation whenever she had to do something. She would for instance go into her bed-room at night, start to take off her dress, put it on again and walk out of the room, and would repeat this three or four times. She would have the same difficulty in going to the toilet, going out visiting, etc.

The past history was as follows: In the family history there was a case of epileptiform seizures in a paternal uncle which came on rather late in life, but otherwise, the family history was negative. In her own history we find that her birth and early development were uneventful. No physical diseases are reported. The history of the sexual development, however, is significant. She had received no information concerning this phase of her life. When she actually asked for information, this was refused and she was told that it was not nice to talk about it. At the age of eight an incident occurred which the patient felt was of importance. She was playing with a girl her own age who had brought with her a doll. This girl playing the part of a mother pretended to nurse the doll from her nipple. When the patient's mother noticed this she appeared very much shocked, scolded both the girls, and told them that it was a very immoral thing to do. When the patient was ten years old a boy in the neighborhood three years older than she, who was known to have had a bad reputation, attempted to force the patient to have sexual relations on three occasions. The patient was frightened and on one occasion became ill, with nausea, vomiting and headache. She did not tell her parents what caused this. When the patient was fourteen, while visiting her grandmother, a cousin, several years her senior, put his hand on her left breast and expressed the idea that she was a grown woman and said to her: "Now you are old enough to have a fellow." The patient was very much upset by this incident. It remained vividly impressed on her mind and was accompanied by a feeling of guilt. She stated that ever since her adolescence she had been conscious of strong sexual feelings. She went out with a number of men, and at the age of eighteen she began to go with a young man somewhat older than herself, whom she liked very much and to whom she became engaged. She broke the engagement later because she felt that he was "too much of a gentleman," and she was not good enough for him. After that she became acquainted with her present husband and later married him. She had sexual relations with her husband before marriage accompanied by pronounced feelings of guilt.

As was stated above, the present condition started eight years before admission while the patient was pregnant with the third child. The patient brought out the fact that these symptoms came on rather abruptly. Her aunt, who had later given her the phonograph, was visiting at that time at the patient's home and

during a general conversation had brought up the subject of the patient's cousin with whom the patient had the above-mentioned unpleasant experience. The aunt jokingly remarked that the patient and the cousin seemed to be attached to one another. The patient who had always been attached to this aunt had a severe reaction to this statement, turned pale, complained of feeling sick, and left the room. Since that time she turned against the aunt and avoided any contact with her. When the child was born she developed her first pronounced symptom, which was a fear of nursing the child from the left breast. Gradually the other fears developed and in the beginning were centralized about this child, but afterwards spread to other objects and individuals. She began to have spells of crying and moroseness, subsequently developing frigidity towards her husband. The arrival of the phonograph from the Aunt seemed to have exaggerated all these symptoms.

The personality, previous to the onset, was described by the relatives as cheerful, easily adjustable and sociable.

Course. On admission to the hospital the patient was distressed, cried a great deal when she talked about her symptoms, expressed the idea of being an immoral person, avoided the other patients, and to the physicians she talked only about her symptoms. She seemed to be genuinely interested in being helped and cooperated very well in the treatment which consisted of discussing her previous experiences, interests and problems with her. It was easy to establish a good contact with her and as the discussion progressed she began to take more interest in outside things and at the same time to lose her fears and hesitations. She remained at the hospital for two months, at the end of which time she was discharged as greatly improved. Her physical condition showed no pathological findings, she was of a rather average physical build, perhaps with a slight tendency toward pyknotic habitus. Her intelligence quotient was 88, and in keeping with her education and milieu. Her progress was followed up for three years after her discharge and she seemed to have adjusted quite well and apparently has remained adjusted up to the present time.

In this case, therefore, we find a clinical picture, characterized primarily by obsessions which the patient knew had no basis in fact and the onset of which seemed to be rather abrupt. Her emotional tone was adequate to the situation, her affect being mostly depressed and anxious. She was genuinely interested in being helped, established a good contact with the hospital situation, and at no time showed any signs of distortion of reality. Her intelligence was average and there was nothing significant in her physical condition. Etiologically, we find no significant hereditary or constitutional factors. The illness seemed to have developed in relation to early sexual traumata in which one of the important factors was a faulty education. The precipitating factors seemed to be related to a re-enactment of the early sexual traumata. Although the picture seems to have developed in close relationship to her sexual adjustment, the level of sexual development seems to have been a normal heterosexual one, with some conditioning factors making it difficult for her to adjust properly. The treatment used here was primarily psychotherapeutic, with excellent results.

When we attempt to evaluate this problem nosologically we find that it resembles more nearly the conditions generally placed under the group of psychoneuroses. The clinical picture, etiological factors, and the most

successful method of treatment are all similar to what we find, for instance, in the cases of hysteria. Among other types of maladjustments, which come in question here, we might mention first the anxiety neuroses, because of the rather pronounced general fear reactions in this patient, and the depressions, because of the marked distress that this patient, and others like her, showed in reaction to their abnormal fears. Both of these features, however, are of secondary importance. From a clinicopsychological point of view, then, we are dealing here with *anankastic ideas*, essentially psychogenic in origin and amenable to psychotherapy.

The situation is somewhat different in another group of cases, a typical example of which follows.

Case 2. E. F. A 25 year old married man was admitted to the hospital with the complaint that for some two years he has expressed a fear of contamination by excreta from other men. Since then he had been showing an increasing scrupulousness in touching people and objects and had continually washed and scrubbed his hands because of this fear. The symptoms were said to have started following an incident when the patient saw another of the farm helpers, a man who had a reputation of being sexually promiscuous, urinating in the barn. He then began to imagine that the dust particles from the barn might gain entrance into the house, get on his clothes, and that he would be contaminated by the man's urine. This then spread to include other men and various types of substances such as saliva, mucus from the nose, etc. When he came into the hospital he began to develop the same fears in relation to some of the male patients and as time went on he began to express the idea that these people actually planned to get these substances on him. His behavior in the hospital was significant and characteristic of this type of patient. He would sit by himself in a stiff posture with his arms held rigidly bent at the elbows. His face was expressionless, almost mask-like, and the skin was glistening. He opened doors and moved objects preferably with his elbows, as he was afraid to touch anything. His productions were sparing, he was reticent, evasive and showed a tendency toward thought-blocking. It was very difficult to establish contact with him, and it was felt that the patient never actually "opened up" freely.

He remained at the hospital for some ten weeks, during which time psychotherapeutic measures, mainly in terms of modified analysis, were undertaken. These brought out the following important facts: He was of an introverted and seclusive make-up. His family history was marked by several instances of pronounced maladjustment, mainly in the nature of psychopathic personality. Early in life he had shown a tendency towards scrupulousness and pedantry. A number of early sexual experiences had occurred which showed marked feelings of guilt in relation to heterosexual acts and an interest in sexual adventures of other men combined with strong attachments to men, and fear of them. His own marriage was more or less forced on him and directly afterward he ran away from his wife. He returned later, but showed very little interest and affection for her. His association during the treatment suggested the presence of a strong homosexual component which was probably responsible for his failure in a proper sexual adjustment. The treatment resulted in some improvement, the patient went home and seemed to adjust on a better level, but his marked scrupulousness, his peculiar personality traits, and the tendency towards fear of other people remained.

In this case, therefore, we find a clinicopsychological picture consisting of compulsory acts which were conditioned by fears of being harmed or

contaminated by things from the outside. The outstanding features were poor contact with the outside, lack of genuine insight, and the search for help was mainly concerned with obtaining comfort rather than actually overcoming the symptoms. The emotional tone was superficially cold with pronounced tension under the surface, and the affect was somewhat stiff and somber. His attitude towards the outside was rather ominous in that there was an attempt to involve the outside in interpreting the reasons for his fears. The significant physical factors were the asthenic make-up and the pronounced, almost Parkinsonian, rigidity of posture and facial expression. The relationship of the disturbance to early sexual experiences is not clear in this case, since it is just as likely that they were expressions of a poorly constituted personality as that they were primary etiological factors. Finally, the precipitating experiences seemed to be related not so much to early experiences as to a probable abnormality of the sexual organization, since we find throughout the life of the patient an under-current of interests which suggest a strong homosexual component. The treatment in this case was unsuccessful and did not result in a satisfactory solution. Finally, when we consider this condition in its relationship to a special diagnostic grouping we find that it goes distinctly beyond the bounds of a psychoneurotic reaction and shows the appearance of symptoms that belong to that group of maladjustments which are placed in the large field of the schizophrenic reaction types. In summing up we might say that here we are dealing primarily with *anankastic activities* and interpretations of reality, which differ fundamentally from the anankastic ideas in the first case.

Finally, we come to another group of cases included in the group of the psychasthenias, an example of which is presented in the following record:

Case 3. J. W. A 19 year old single man was admitted to the hospital with the complaint that he had been having "peculiar thoughts and fears" of which he could not rid himself. They consisted of obsessive thoughts of mutilation of himself and others, feelings that he was unreal and transparent and thoughts that "things outside were changing with the season," that there was "no law of gravity" etc. These symptoms interfered with his work because, as he stated, his thoughts seemed to be "cut off" once in a while and he would have to stop the work or conversation in which he was engaged at the time.

An analysis was undertaken in this case and this, combined with the history obtained from the outside, yielded the following facts: The family history showed a high incidence of mental disorders. The patient himself had always been regarded as "peculiar," rather shy and a poor mixer. Within the last few years, however, his quiet and unusually scrupulous behavior was interrupted occasionally by the occurrence of impulsive outbursts and strongly sadistic tendencies. Although the present symptoms were supposed to have developed recently, it was ascertained that as far back as the age of 4, the patient had had compulsive tendencies and obsessive thoughts. His sexual development was characterized by a strong fixation on his mother and a subsequent transference of this to an aunt who had encouraged him to indulge in sexually colored play with her. At the age of puberty following the development of autoerotic practices, he began to show feelings of disgust and guilt

in relationship to sex in general and then developed feelings of unreality which recurred at intervals up to the present time. Thus the symptoms that brought him to the hospital were found to be exaggerations of, and superimpositions upon, traits which had really existed all through his life, although they had only recently begun to interfere with his work. Running parallel to these experiences was a gradually increasing tendency to ruminate about things, especially his own thoughts and sensations. There also had been a marked preoccupation with his physiological functions, especially the gastro-intestinal ones, and an interest in the development of his muscles. He read about anatomy, analyzed his feelings and thoughts with hair-splitting scrupulousness and showed an unusual conscientiousness and pedantic carefulness in his work.

In the hospital he gave the impression of being a cold, reserved and serious-minded person. It was difficult to gain contact with him. His answers were short and precise and he made no spontaneous statements. In the analysis, however, he showed a great deal of pent-up emotion and a strong push of free associations. Both were related to underlying sadistic fantasies concerning himself and others, and his own physical sensations. A prolonged analysis undertaken in this case showed definitely that a series of psychic experiences had preceded the gradual development of his present reaction. These experiences went back so far in his life, however, and were so closely related to early character traits that it was a question how much they were the direct outcome of a faulty personality rather than the cause of the present condition.

In this case, therefore, we deal with symptoms that developed so gradually and reached so far into the early childhood of the patient that it is almost impossible to differentiate them from early character traits. When we add to this a family history heavily laden with mental abnormalities, we find ourselves forced to assume a strong constitutional basis. In the clinical picture we find, primarily, *anankastic traits* consisting of doubts and obsessions, an emotional tone which is cold and formal, and an objective, impersonal attitude toward the disease. The contact remains on a superficial, intellectual basis, and the search for help is really a rational inquisitiveness. Physically the patient was of the asthenic-athletic type, with a stiff and mechanical posture. Finally, we must add that the treatment produced practically no results and after several months of study in the hospital the patient continued to progress in his obsessive, ruminative activities and at present is showing a tendency which makes one think again of the schizophrenic type of reaction. Nosologically, this patient seems to be more closely related to the schizoid psychopaths than to the psychoneurotic group.

Of the twenty-eight cases studied, we find that ten belonged to the group characterized by the features presented by the first case, eight to that characterized by the features described in the second case and five were similar to the third case. The others showed a mixture of symptoms with a predominance of one or the other type.

Thus, we find that this series of unselected cases of psychasthenia shows a number of fundamental differences which justify a division into separate groups, primarily distinguished on the basis of the characteristic clinical

features but which show, at the same time, important variations along the following lines:

1. Probable etiological factors and peculiar manner of development of the symptoms.
2. Therapeutic results and indications.
3. Prognosis, especially as established on the basis of follow-up investigations.
4. The relationship of these clinical pictures to other forms of mental disease.

To facilitate a general survey of these factors, I have tabulated in the following two charts, the most important clinical, etiologic and therapeutic features as they occurred in the cases belonging to the different groups. These characteristics are not to be taken as belonging to any one single case but represent a reconstruction of the most frequently encountered manifestations in the cases belonging to the particular groups. In Chart I the results of the clinical analysis have been tabulated. As can be seen, the most striking differences occur between Group I, on the one hand, and Groups II and III, on the other. This difference consists primarily in the fact that the last two groups, in contrast to the first, show the first indications of those psychopathological phenomena which, when fully developed, serve as the distinguishing marks of the schizophrenic reaction-types. Thus, for instance, we see that the affect and emotional tone in the first group are adequately related to the situation whereas, in the second and third, they become stiff and cold toward the outside, but with a good deal of tension related to the patient's own ruminations. Similarly, we note the good contact that the patients in Group I have with their surroundings in contrast with the poor, or, at best, superficial, contact in the others. In close relationship to these phenomena we find in the last two groups, a definite tendency toward distortion of reality, shaping and coloring it by suspicions, depersonalizations and sometimes, projections. This is particularly clearly seen in the difference in the central symptomatology. In the first group, the obsessive thoughts generally remain within the person himself. It is *his own* thoughts from which he cannot free himself, *he* may harm himself or others, etc. In the second group we find, first of all, the spread of these ideas to involve the outside. That is, the contamination, bacteria and other substances, come from the *outside* to affect him. In some cases, this trend of thought attains the seriousness of actual delusional formation wherein people on the outside are purposely planning to harm the patient by contamination or infection. Another significant feature here, is the frequent occurrence of compulsive acts which, upon analysis, can be found to originate in an attempt on the part of the patient to counteract his fears and suspicions by some outward act. In other words, he treats his anankastic fears as if they were based on reality. In both groups, particularly in the third one, we find furthermore, a good deal of

rumination and introspection which must be regarded as equivalent to autistic thought. Thus we see that the function of "subject-object differentiation" which is so necessary for normal behavior, and is rarely, if ever, lost in the true psychoneuroses, is quite definitely involved in the last of the two groups.

Among other differentiating features of importance we should note the fact that, whereas the patients in Group I show a sincere and earnest desire to be helped, those in the second group are only interested in securing superficial comfort with a preservation of their symptoms. In the third group we meet with an empty, coldly objective inquisitiveness as if the

CHART I
Clinical Analysis

CLINICAL FEATURES	GROUP I	GROUP II	GROUP III
1. Onset	Rapid to abrupt	Usually slow	Chronic, from early childhood
2. Chief symptoms	Obsessions; fears of harming others	Compulsive acts; fears of being harmed or contaminated by others	Doubts; obsessive thinking; intellectualization
3. Reality distortion	None	Suspicious; fears; depersonalizations; projection	Depersonalization; autistic thinking
4. Subject-object differentiation	Not involved	Decreased	Exaggerated
5. Emotional tone	Labile but adequately related to symptoms	Superficially cold with underlying tension	Stiff, formal, cold; (? of underlying tension)
6. Affect	Depressed; anxious	Somber; anxious	Serious; inquisitive and objective
7. Contact	Good	Poor or difficult to obtain	Intellectual; not affective
8. Search for help	Usually sincere	Superficial comfort with preserved symptoms	Only on rationalizing basis
9. Intelligence quotient.	63-114	72-113	85-122
10. Age	13-46 years	25-42 years	14-34 years
11. Physical type	Mostly average; pyknotic tendencies	Mostly asthenic	Asthenic, athletic
12. Physical anomalies	None	Some dysplastic features	Some dysplastic features
13. Posture	Not affected	Stiff or rigid, reminiscent of Parkinsonism	Stiff and mechanical
14. Motor concomitants.	Rare; if present, related to mechanisms	Frequent; related to symptoms	None

patient were an outside observer, simply interested in discovering various logical relationships, rather than having an emotional interest in securing help.

Physically, the last two groups usually consist of asthenic and athletic persons as contrasted with the fairly average type of body build which is encountered in the first. An interesting feature which is particularly frequently met in cases belonging to the second group is the rigid, almost Parkinsonian posture and lack of facial expression.

It would seem, therefore, that whereas the clinical picture of the cases belonging to Group I can be regarded as essentially psychoneurotic in type, the other two definitely overstep the bounds and reach far into the realm of

the schizothymic or even schizophrenic reaction-types. This cleavage can be followed equally well in the analysis of the etiology (see Chart II). In the first group we find patients who show a minimum of hereditary tainting and few pathological constitutional characteristics. In keeping with the manner of development of other psychoneuroses we find here definitely relevant early psychic traumata and a clear relationship between them and the precipitating factors. Contrasted with this are the more ominous rôles played by heredity and constitution in the second, and

CHART II

	GROUP I	GROUP II	GROUP III
Etiology			
1. Heredity.....	Predominantly negative	Tainted to heavily laden	Heavily laden
2. Constitutional traits.	Average; some shy or "nervous"	Poorly adjusted; obsessive personalities	Definitely abnormal personality
3. Level of sexual development.....	Heterosexual; some substitute phenomena	Latent homosexual or other deviations; heterosexual attempts unsuccessful	Latent or overt homosexuality; narcissistic; some apparently hyposexual
4. Early causative factors.....	Sexual traumata; poor home conditions	Occasional traumatic experiences—uncertain whether effects or causes	Onset so early that few preceding factors can be elicited if present
5. Precipitating factors	Re-enaction of early traumata; marital, social, economic difficulties	Attempts at sexual adjustment, economic or social difficulties	Difficulties in home or social adjustment; attempts at sexual adjustment
Treatment			
1. Methods used.....	Explorative; psychoanalysis; suggestion	Explorative; suggestion; psychoanalysis	Explorative; suggestion; psychoanalysis; correction
2. Results.....	Good to fair	Fair to poor	Poor to none
Prognosis and Nosological Relationships			
Prognosis.....	Good	Doubtful	Poor
Nosologic Relationships	Hysteria; anxiety neurosis; depression	Schizophrenia and schizothymic reactions	Schizoid psychopathy

particularly in the third, groups. In fact, it is here that we find the main difference between the second and third groups. Although superficially similar, they really differ in that the second group has more of the "process" quality, whereas the third must be regarded as the exaggeration of a constitutionally defective personality. It is for this reason that, nosologically, the first group should be considered as clearly within the limits of the psychoneuroses with, perhaps, some of the aspects of psychogenic depression. The second group seems to lie on the borderline between the psychoneuroses and schizophrenia and approaches the latter so closely,

at times, as to raise the question whether they should really be placed in this group. Finally, the patients in the third group seem to be most closely allied to the schizoid psychopathies.

I should like to emphasize again that this differentiation within the field of the psychasthenias is not a matter of mere didactic hair-splitting, but is of importance in the practical aspect of our work. This is shown first of all in our experiences in the treatment of these patients. As can be seen in Chart II, the various psychotherapeutic measures undertaken were usually successful in the case of patients belonging to Group I. Given the proper conditions, therefore, the prognoses are reasonably good. In the second group, for the most part, psychotherapy met with as much success as one finds in some of the milder psychoses. In fact, one wonders whether the danger of causing more injury by stirring up latent homosexual and other character deviations by using the treatment usually followed in the psychoneuroses may not more than offset any possible help the patient might obtain. Finally, in the third group, the results were practically negligible.

CONCLUSIONS

The above analysis of our material permits the following statement in answer to the queries posited in the introduction: 1) Anankastic symptoms are encountered in all psychasthenic syndromes and should be regarded as the central feature of the maladjustments, in contrast to other forms of mental disturbances in which they are accessory or secondary in nature. 2) This, however, seems to be the only important link between all the cases in this series. In all other respects, viz., the general clinical picture, the manner of development, the relationship of the symptoms to the underlying personality, background, etc., the differences are so fundamental and far-reaching that we must consider this series as divisible into three separate groups. 3) From a practical point of view it is important to appreciate the fact that the methods of treatment to be employed and the success which they are likely to meet, depend to a large extent upon which of the three groups a particular case belongs to. 4) These separate groups seem to show close nosological relationships to certain forms of established disease entities. At present, however, it is questionable whether a definite realignment in classification should be undertaken, since further work with a larger number of cases and more intensive analyses will be necessary before any definite statement can be made in this connection.

THE NOSOLOGICAL STATUS OF PERIARTERITIS NODOSA

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Ever since the original publication of Kussmaul and Maier (1), reports of cases of periarteritis nodosa show a progressive increase, so that it is no longer regarded as a rare malady. Most of the reports are casuistic and, aside from the establishment of numerous clinical concepts, little has been added to the understanding of the malady. Certainly its position in nosology has not been determined. The following case report illustrates the difficulty of the problem.

E. B., a female, aged 52, was admitted to the Service of Dr. B. S. Oppenheimer on October 1, 1937. The family history was irrelevant, and, aside from an attack of pneumonia nineteen years previously, she had always been well. About a year before admission to the hospital she developed transient pains in both feet. Five months prior to her admission she was told at the New York Hospital that she had "arthritis." This was treated by injections, with some relief. At that time, her blood pressure was normal. Soon after she noticed on exertion some shortness of breath and palpitation. Three months previously she noted swelling of the legs which would abate in the morning. The "arthritis" became worse, so that she tired easily. Five weeks ago she had an attack of diarrhea with eight to eighteen stools a day, which were not bloody. She noted a pruritic eruption of both thighs. These lesions gradually disappeared, but recurred a few days ago. About one week previous to admission she had fever, malaise and a cough with whitish sputum. Nine days ago she was told for the first time that she had an elevated blood pressure, and albumin, pus and blood were noted in the urine.

On examination, there was edema of the eyelids and conjunctiva. There was a moderate papilledema with hemorrhages in the retina, but no exudates. The blood pressure was 190 systolic and 120 diastolic. On the right thigh there were fairly large patches of fresh hemorrhages in the superficial skin and a few urticarial wheals. In addition, there was dermatitis of both legs. The urine contained two plus albumin, and showed a lowered concentration. The hemoglobin was 58 per cent; the red blood count, 3,310,000; the bleeding and clotting times were normal. The Tourniquet test was negative. There was a small amount of fluid in both pleural cavities. The heart revealed no abnormality. The electrocardiogram revealed myocardial involvement. A spinal tap showed a pressure of 190 mm. of water; the fluid was hemorrhagic, containing crenated red blood cells. A number of spinal taps done in the course of the next two or three weeks revealed the same findings, but a few days before death the spinal tap became clear.

The bizarre picture of the disease and the presence of the cutaneous lesions suggested the possibility of periarteritis nodosa and a biopsy of the deltoid muscle revealed the typical lesions. About three weeks after admission evidences of left ulnar neuritis developed. At no time was the blood urea elevated. The course of the malady was progressively downward and she died on November 9, 1937. No autopsy was permitted.

It is evident that the only clinical diagnoses possible in this case were acute glomerular nephritis and periarteritis nodosa. The problem now confronts us as to whether we shall regard this case as one of glomerulonephritis complicated by periarteritis nodosa, or as one of periarteritis nodosa complicated by glomerulonephritis. In other words, is periarteritis a primary disease, or is it merely a complication, or a superimposed lesion?

This case is by no means unique in this respect, because this very problem of the nosological status of periarteritis nodosa confronts us in the majority of instances in which this lesion is encountered. Inasmuch as periarteritis nodosa is notoriously associated with such protean clinical syndromes and is so rarely encountered as a pure unalloyed lesion, the suspicion is at once aroused that periarteritis nodosa is, in most instances, a complication or a secondary lesion and not the fundamental disease. In order to test the validity of this suspicion, the records of nineteen cases of periarteritis nodosa observed in The Mount Sinai Hospital were carefully checked. Seventeen of these cases were reviewed by Dr. Rose Spiegel (2) in a recent excellent and comprehensive publication. Two of these cases, which clinically simulated acute appendicitis and which recovered, must obviously be excluded from consideration. Of the remaining sixteen cases which came to autopsy, three revealed the lesions of rheumatic fever with typical Aschoff bodies and the characteristic valvular vegetations. These cases have already been reported by Gross and Friedberg (3). Two cases presented the characteristic clinical and morphological picture of malignant nephrosclerosis. Two revealed the clinical and morphological changes of glomerulonephritis. Two cases followed sepsis arising from acute sinusitis. Three patients presented the clinical picture of hypertensive disease with albuminuria and renal insufficiency. One case was a typical disseminated lupus erythematosus. In only three cases could the clinical manifestations and the anatomical findings support the contention that the lesions of periarteritis presented the only existent malady, a percentage of 18.7 per cent.

It seems, therefore, that in the vast majority of instances, periarteritis nodosa is a complication or a superimposed lesion, and not the primary event. This view does not deny the fact that the lesions of periarteritis nodosa complicate the clinical picture very profoundly, either by aneurysmal formation, hemorrhage or thrombosis; nor does it settle the mysterious etiology of the lesion. There is much clinical evidence suggesting that periarteritis nodosa represents an allergic vascular reaction. In her paper, Spiegel has summarized this evidence. More recently Clarke and Kaplan (4) describe lesions closely resembling those of periarteritis nodosa following serum disease. However, the allergic etiology requires much further study before it can be accepted.

In terms of analogy, therefore, periarteritis nodosa must be viewed clinically and morphologically, as we do pleurisy. Pleurisy is only very

rarely a primary phenomenon; we do not speak of pleurisy complicated by pneumonia or tuberculosis or rheumatic fever, but conversely.

SUMMARY

Periarteritis in the largest majority of instances is not the primary clinical or morphological entity, but a complication of various widely divergent clinical and morphological backgrounds.

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TIME AND PURPOSE

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One of the fundamental implications of reality is awareness of present time, for the future and the past are comparatively unreal. Neither time nor unreality manifest themselves with a material existence. Nevertheless, individuals react to this immaterial existence of time as though it were an actual object, much in the manner they assume toward the feeling of unreality.

In considering time and kindred phenomena of reality, a definition of the latter, difficult as it may be, should be attempted. The concept of reality includes both the feeling that the person himself is real and the world around him is real—a real person in a real world. The feeling that one's own body is real is usually taken for granted. It is dependent upon the continuous integration of perceptions of stimuli flowing from external sources and internal sense organs to that part of the body which registers them. Presumably the function of registration rests in some portion of the nervous system. Apparently the sense of somatic reality is an unconscious, as well as conscious, phenomenon. When this registration is constant and clear, it yields a sense of the normal functioning of the organs of the body to which the term *coenesthesia* is applied.

The outside world is real to a person when the impressions which he receives from it through the five senses are not seriously questioned. The roll of a drum, the color of trees, the prick of a pin or the form and quality of another person are registered regularly as actualities which may change from time to time in degree but are never seriously doubted. Fluctuations in the degree of reality perception in the same person presumably in the same physical condition occur and may transiently give way to feelings of strangeness or unreality.

Pathological disturbances in both spheres of reality appreciation can occur. The person's entire body or any part of it may appear to him as unreal. To this condition the term *depersonalization* has been applied. The outer world may appear unreal to an intact "body-total". For this condition of vagueness or unreality of the world or things in it the term *derealization* has been suggested by Mayer-Gross (1). It is to be expected that *depersonalization* and *derealization* may occur in the same individual, although the patient usually places the major emphasis on one phase or the other.

In all probability the earliest concepts of time depend upon somatic stimuli reaching the child from within. Perhaps the earliest automatic repetitive time movement is breathing. This is from birth so automatic (unconscious) that only when something interferes with the short, regular time interval between inhalation and exhalation does the person become aware of this early acquired time perception. Breathing time is soon followed by time sensations in connection with feeding and evacuation, sleeping and waking.

Reminders of this intrasomatically determined concept of time are reflected in our language, such as "breathless haste," "quick as a wink," "bed time," "waking time," or "my stomach tells me it is dinner time." A further preservation of the concept of time in terms of body function is found in menstruation being "regular as clock work." Of course, in the later development of the sense of time external stimuli, such as light and darkness, temperature and weather sensations, play a strong and obvious rôle.

The concept of time like the concept of space is certainly not exclusively, if at all, a phylogenetic inheritance, but derived mainly through individual experience. As acquaintance with time becomes familiar, the individual develops various and varying attitudes toward it. While we do not inherit a sense of time, most likely our earliest impressions of it are dependent upon our individual past experiences, such as already mentioned in evacuation and breathing, fortified by incidents connected with them. Such impressions have little to do with the future. This is evident in both the somatic and extra-somatic stimuli.

Normally the present is finite and real. The distant past and the remote future are generally each divested to a certain degree of the element of reality. So it is not surprising to find in patients in whom the sense of reality is pathological that abnormal reactions in regard to the element of time also occur.

Patients suffering from depersonalization may complain that they are living in the abstract, or that time has no meaning for them. Time may appear very much condensed, there is a lack of perspective so that hours seem like a few minutes. In extreme cases the present is less real than the future or the past and the present may be only a means of marking time for the future. Some patients in this class may have a strong sense of small elements of time to make up for the absence of any real time sense—trying to satisfy themselves with the letter instead of the spirit of time. They may develop an actual fear of the present time and its reality implications with a relative confidence in the remote past or the remote future, or a tantalizing uncertainty concerning the immediate future or the immediate past.

The feeling of being pressed for time, or of time being pressing, is due to

interest in the appropriate employment of time.* This regard for accomplishment and achievement, or making what some persons regard as the greatest use of time, is governed by higher intellectual and ethical strivings which compose the super-ego category of personality. Harnik (2) has called attention to the unconscious connection between the concept of time and the super-ego or ego ideal which, in his opinion, essentially represents a father identification.

In considering time, Mary Sturt (3) has pointed out that the development of the concept of the future depends mainly upon purpose, although memory has some influence on it. The future is an unfulfilled purpose which has a conscious aim, and anticipation is concerned with the completion of purpose. It is the present writer's belief that persons showing great anxiety in connection with time suffer from unusual conflict of purpose, in addition to their inexorable drive to make use of time.

From the standpoint of fulfillment of ideals a suspension or abolition of time would exclude the possibility of giving a direction and purpose to life. "Killing time" is a suspension of purpose, temporarily at least, and may represent an immediate or transient defiance of the directing function of mind and purposive thinking.

The average person's thoughts, purposes and actions follow in close sequence—especially those which concern the innumerable minor activities which make up a day's events. In such people whose purposes and acts cause relatively little reflection, time is taken for granted. In contrast to persons who are indifferent to thought value or who have a tendency to laziness, a person who has eroticized thinking has a higher regard for time. He is under the domination of an insistent super-ego urging him on to accomplishment. Elsewhere I have pointed out that the quality of thinking, super-ego function, may be regarded by the child as a masculine or feminine attribute (4).

In a case studied for several years the patient's difficulty in thinking was intimately associated with uncertainty as to purpose and future. The present seemed less real to him than the future even though normally the present usually involved something concrete and the future was abstract. The future seemed clearly identified with his mother's goals and aims which he had incorporated into his own personality as an absolute guiding force. Moreover, the patient identified the concept of the past, as well as the future, with his mother. The present, which he tried to avoid, carried with it the dangerous element of reality which to him was masculine striving.

In the case presentation I shall attempt to interpret the patient's

* For purposes of this paper it is unnecessary to go into details of the psycho-analytic associations between ano-erotism, the saving of time and money and its effect on character formation and attitude toward time.

disturbance in thinking and its relation to his confusion in regard to present time. This latter, in turn, depended upon his unconscious associations involving future time, purpose and super-ego formation. A limited description of the circumstances under which the concern with time and achievement developed included the following data:

CASE REPORT

The patient, aged nineteen when he entered analysis, was the member of a once comfortably situated middle class family, whose economic position had been severely affected by the depression of 1929. His father, a college graduate, had drifted through life because of a fortuitous inherited social position. However, his authority in the home circle was quite negative.

The mother was a self-assertive, energetic, ambitious and superficially competent woman, absorbed in the attainment of social and business prominence. To the patient she seemed highly intellectual and intelligent, especially when judged by her bridge playing. He did not fully appreciate, until he himself became a good bridge player at seventeen, that his mother's thinking was badly muddled and that she had appeared intelligent to him merely because she had asserted herself loudly.

From his earliest memories the patient had been the object of his mother's attention and training. This solicitude and incessant supervision continued up to the time he went to college. A variation from the usual pattern of close attachment between mother and son consisted of long conversations concerning activities and anxieties for the future. These conversations began late at night and often continued until early hours in the morning. The mother, usually in her nightgown, because she had already prepared for bed before going to her son's room, would complain of her husband's ineptitude in life and spend the night in discussing plans whereby the patient might attain higher and higher standing in his studies. This had now become her main purpose in life so that she might exalt herself through his brilliance in the future.

The patient showed intellectual precocity from infancy and developed in a normal way physically. A peculiarity in conduct, caused by a hesitation in making decisions, which in turn produced an inability to act decisively, made him the butt of other boys from the time he began to mingle with them. In play with little girls he had less difficulty. Because he was afraid to fight, he became the object of ridicule and abuse and was usually excluded from boys' games, although he desired to join them.

In school his advancement was rapid, his performance and scholarship excellent. It is difficult to determine how much his success was due to innate intellectual superiority and how much depended upon a neurotic sublimation of his talents at the instigation of his ambitious mother. Even when his grades began to fail in high school he was regarded as an extraordinary student, especially in mathematics.

The patient had been compelled to leave college in his sophomore year, interrupting what had promised to be a brilliant career. He suffered from blind outbursts of confused rage, inability to concentrate and to think consecutively, and a concomitant profound depression.

COMMENT

As in so many other cases of this type, a psychiatric classification of his condition could have placed it in either the manic-depressive or schizophrenic group. The prominent symptoms of agitation, depression, self-

accusation and retardation in thinking would have spoken for the former; his tendency to retire from association with his classmates, lie in bed all day, his negative and stolid attitude toward his family, and his intense antagonism toward his parents, at times verging on ideas of persecution, would have warranted the diagnosis of incipient schizophrenia. Other psychiatrists, acquainted with the patient placed his malady in the schizoid group, which is perhaps the best way of classifying the case.

A long psychoanalytic investigation revealed that the connection between the immediate present and masculinity went back to the patient's earliest contacts with little boys. They acted quickly, directly, combatively and decisively and he felt compelled to conduct himself in a similar manner if he were to survive. That was the way of boys. The direct opposite was the manner in which it was desirable for him to act if he wished to follow the pattern of his mother, which was the equivalent of pleasing her.

With her, according to the patient, nothing was ever done in the present. All her thought and attention were devoted to a review of his mistakes in the past and meticulous planning for the immediate future. A reaction formation to this tendency of his mother to consider only the future and the past arose when he was called on to mobilize past experience for the benefit of present activity. Thus, whenever he attempted to think and to draw on previous experience to enable him to make immediate decisions, his mind tended to stop operation, sometimes becoming entirely blocked.

Often undertakings, even relatively simple ones, appeared to be impractical or too difficult of attainment because of a conflict in purpose whether or not to proceed with them. Time, like his mother's supervision, was something which he felt he must overcome. He must make up for lost time and for his mistakes in the past. The latter merged imperceptibly into the present which he had identified with masculinity. Time, like his submission to his mother's purposes, became an autocratic master dominating in a cruel manner his entire life. His fight with time, in which time usually overcame and punished him, constituted a veritable threat to his existence.

The patient tried to crowd things into an impossibly short space of time in order to goad himself along more forcefully. There was an actual effort to extend time or make more time in order to do more, particularly after he felt that he had been loafing or after he had seemed to have failed to do his best. Sometimes he tried to crowd and rush things in order to evade the consideration of some difficult point or phase of a problem.

If a certain goal were set for him by someone else, his mind, using a mechanism akin to introjection, was compelled to manipulate it so that he felt as if he himself had set that goal. For example, a friend would say that the patient should meet him at three o'clock. Then it often seemed to the patient as if he, or perhaps his mother, had set the time and there-

fore he was responsible for it. This responsibility became his own by virtue of the fact that if he had not allowed himself to become acquainted with the friend, the question of an appointment would never have arisen.

The responsibility would be further increased because he had taken the initiative or had allowed the acquaintanceship to occur without his mother's suggestion or authority. Thus it became he who had set a time for the appointment—really a purpose and time limit—for himself. This type of assumed responsibility demanded action in the present and he could never fully and freely accomplish it. It lacked the approval and assurance of his mother whose commitments always took the form of future achievement.

The patient was often late for appointments, partly because of a compulsion to place himself in a situation where the limited time would force him to attempt to accomplish more than could reasonably be expected of a normal person. To counteract such dilemmas, at times, he tried to disregard his shortcomings entirely and to arrange things as he felt a normal person would, but really he sought the speed and perfection that only a super-being could attain.

So, too, he often forced himself to meet situations entailing prolonged difficulties by trying to do too much in a short space of time. This spurred him to increased action up to the point where the problem became too difficult. Then his thinking processes would break down entirely and he would evade the question. If this forcing of activity in achievement against the feeling of time's passing went far enough, he lost his concept of time entirely and felt himself hopeless, uncertain, unreal or even dead.

A corollary of this loss of time sense in him, with its accompanying unreality and numbness, was the feeling that life was not worth living. This, in turn, led to constant threats of suicide. Then he needed reassurance from an outside source which represented reality, because, being half dead and unreal, he was unable to guide himself.

When his personality became too dualistic because of inability to meet the present and a compulsion to act in the present, he became fearful and could not plan for the future. To think and act in the present, as already stated, was masculine to him and inability to meet the present was feminine. Planning for the future was equivalent to submission to the maternal mode of action, namely to a feminine super-ego which had developed as a result of the long identification with his mother. At these times the conflict between his masculine ego and feminine super-ego compelled him to reject such direction and he became confused. His own personality could again become coordinated only after reassurance from without, such as also became necessary when he attempted to hurry his thinking against time.

This need for aid was the unconscious reason why, before analysis, he still constantly sought contact with his mother, even though he hated

her to such a degree. It also accounted partially for his mental debacle at the time when he went to college, where such contact with his mother became impossible. The mother, reluctant to relinquish control, discouraged him from any purposes other than those which she would approve. To him her attitude represented disapproval of present activity and encouragement for the future.

As a result of treatment, his own masculine guiding force developed more fully, enabling him to turn away from his mother's direction. At the same time his guiding force gradually began to approximate his acting force, in other words, the relation between the two became more nearly normal.

To counteract his tendency of forcing himself to super-activity by crowding many acts into a short time, he had fantasies reaching into the distant future. In these fantasies he would imagine himself very active over an extended expanse of time. His happy fantasy of successful accomplishment in the far future sometimes encouraged him to carry on in the present. Another helpful fantasy for sustaining him in the present was the imagination of having been in extraordinary difficulty in the immediate past.

He found it impossible to do exact things not requiring abstract thinking, such as remembering poetry. The abstract in thinking, as in concepts of time, borders on the future infinite in contrast to the present finite. He hesitated to do or say anything for which he could be too specifically criticized. This would leave him no alibi in case of inaccuracy for then he would be confronted with cold facts out of which he would not or could not rationalize himself.

When his mother found herself faced with an irrefutable fact, she made an illogical, obviously false explanation which seemed to satisfy her, even if no one else believed it. Whether she actually believed most of her ridiculous explanations he did not know, but he did discover that they saved her self-esteem in the absence of critical faculties concerning herself. Because of a certain logic in his reasoning it was difficult for him to get relief in this manner when proved wrong. In contrast to his mother he, at least, consciously admitted his errors. Notwithstanding their similarity in many ways, he could not defend his mistakes with false logic and felt nervous and insecure when in the wrong, similar to the anxiety already described when he attempted to crowd the present, or acted in a way contrary to his mother's purposes.

It appeared to him that things done just for the moment gave little satisfaction and that things done for too ultimate a purpose were equally lacking in substance. After considerable treatment the patient became freed of the identification of his own super-ego with his mother's and of considering the future only in the light of his mother's purposes. He

gradually realized that living was a day-to-day, really a minute-to-minute, affair; that today's actions and activities were as important as those of days to come. He planned less for a vague ulterior purpose far removed from concrete activity.

That the real feeling of satisfaction is dependent upon acting in the present, planning for the future and understanding the past came to the patient very slowly. Balancing the value of the three was far more difficult for him than for most people. At a given time he could not tell whether he would be motivated by the impulse to act and think in the present or by the counteracting impulse to moon and dream of the future. Often this conflict caused him to hesitate when he might become involved in situations where he might have to battle with a strong unconscious desire to act in a purposeless, infantile manner when thought and directed action were demanded.

Because of his desire to avoid doing things with great exactness which he felt might expose him to legitimate criticism, he was unable to appreciate normal leeway in action and was compelled to follow the letter of the law exactly—like a child. To him, wrong action carried with it a literal death punishment. On the other hand, when legitimate liberty existed for using his own judgment, he failed sometimes to take advantage of it for fear of incurring his own (unconsciously his mother's) harsh criticism. This had often been the case in the past where he had made mistakes when the path of action, at the time, had seemed unquestionably clear to him.

SUMMARY

In the above presentation an attempt has been made to show how conflict with purpose affected the patient's ability to cope with time, and how the entire moulding of his own purpose was based upon his mother's concept of purpose. As long as it was possible for the patient to maintain faith in the integrity of his mother's own thinking, that is in her purposes, he could maintain himself fairly well in life's struggle. This was so, notwithstanding the painful difficulty he experienced in attaining a normal position in his social group, especially as a boy-child and school-boy, where purpose and present time were practically one. To a certain extent he was able to lessen his difficulties in the present by recourse to abstract thinking, such as mathematics, in which there was little need for action. When he finally lost faith in the reliability of his mother's feminine future and found it incompatible with the demands of the masculine present, he became confused, unable to think and felt unreal.

This excerpt from a case psychoanalyzed over a period of years seems to support the theory that the concept of future has its origin in purpose and goal, which are so largely incorporated in the mind as a result of parental identifications.

Here the temptation arises to speculate on the increased tempo which pervades modern life. For a world, composed of individuals, an increas-

ing number of whom are in pursuit of more and more difficult ideals, must hurry if it is to reach these goals. This speed in turn, may be an additional factor in the development of unsatisfactory compromise formations and neurotic conflicts which many psychiatrists think are on the increase today.

Both goal and purpose, perhaps hopes of immortality, primarily determine the concepts of future time. It appears that a balanced concept of time is dependent upon a relative unity in purposive strivings. Achievement of purpose harmony acts as a complement to a fuller attainment of goals in that short span for which there is a time limit called death, when, so far as we know, conscious purpose ceases.

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OBSERVATIONS ON THE EFFECTS OF LIVER EXTRACT IN PERNICIOUS ANEMIA WITH SPECIAL REFERENCE TO THE PARAPLEGIC FORM OF SUBACUTE COMBINED SCLEROSIS

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Since the introduction of liver extract by Minot and Murphy (13) in 1926 for the successful treatment of pernicious anemia, a great opportunity has been offered for study of the effects of this treatment on degeneration of the spinal cord associated with the disease. There appears to be some difference of opinion concerning its efficacy in arresting this process and in effecting healing and restitution. The early reports by Sturgis, Isaacs and Smith (18) Cohen (4), Seyderhelm (16), Curschmann (6), Grinker and Kandel (9) and others were not favorable. Schaller and Newman (15) attribute this to inadequate treatment. These investigators and Strauss, Solomon, Schneider and Patek (17), Mills (12) and others believe that adequate treatment of such cases, especially with the parenteral form of liver extract, results in arrest, improvement or prevention of the neuropathic symptoms. However, in all the reported cases of subacute combined degeneration it appears that sufficient emphasis has not been directed to the paralytic form of that condition. The purpose of this paper is to present the results of an investigation in this type of neuropathic involvement, and evaluate the effect of liver therapy in its arrest and improvement.

REPORT OF CASES

Cases may be divided into four main groups.

The first two subdivisions deal with successfully treated cases who had frank paralyses on first admission and those who developed paraplegias in relapses due to negligence of treatment. The latter two groups deal with cases without response, due to inadequate therapy or refusal of it, or because of death before sufficient therapy could be administered.

Group I. Paralytic cases who received no prior treatment and showed a favorable result after liver therapy.

Case 1. (Adm. 270313). A Canadian housewife, aged 33, was admitted to the service of Dr. I. Strauss, August 1926, complaining of progressive numbness of the hands and feet and paresthesias for one year. Three weeks before admission the

patient slipped from a horse and sprained the right ankle; about one week after this occurrence the tongue became sore.

The general physical examination was negative. The neurological status showed a marked ataxia, slight hyperreflexia of the right ankle and knee jerks, diminution of the position sense in the lower extremities, and loss of vibratory sense up to the sacrum.

The blood picture was typical of pernicious anemia: -hemoglobin, 90 per cent; red cells, 4,050,000; color index, 1.1. There was an absence of free acid in the gastric contents.

After a short stay in the hospital, the patient was sent home unimproved. She was not seen again until the early part of November 1926 when she was found to be bed-ridden and incontinent. The anemia had become more severe. The hemoglobin was 60 per cent and red cells were, 2,480,000. The patient was advised to eat a half-pound of liver daily. Under this regime there was gradually a return to normal. The improvement in neurological involvement was very slow. The incontinence subsided first and after a few months the patient was able to stand with the aid of braces and crutches and finally was able to walk with assistance.

Case 2. (Adm. 289530). A Scotch housewife, aged 68, was admitted to the service of Dr. B. S. Oppenheimer April 28, 1928 complaining of increasing weakness and pallor for six months, paresthesias of fingers and toes and soreness of the tongue. Shortly before admission her weakness became so severe that the patient was unable to walk and became bed-ridden.

Examination revealed a marked lemon-yellow pallor and atrophy of the papillae of the tongue. The neurologic findings showed absence of deep reflexes in upper and lower extremities, bilateral Babinskis, marked ataxia of the lower extremities, and the absence of vibratory and position senses.

The blood picture was that of a severe macrocytic anemia with a hemoglobin of 28 per cent, red cells, 1,200,000. The gastric contents showed no free hydrochloric acid.

The patient was given liver extract orally and made a slow but progressive recovery while under observation. The blood picture returned to normal. There was a gradual increase in strength and a reappearance of the deep reflexes. She was able to walk with assistance before she left the hospital.

Case 3. (Adm. 372501) A housewife, aged 42, was admitted to the service of Dr. I. Strauss, October 2, 1934, complaining of progressive weakness in the legs of one year's duration. Following a thyroidectomy two years previously, the patient experienced paresthesias of the fingers and toes, which persisted and was followed by gradual loss of power of the lower extremities. Some liver extract was administered orally but this treatment was not long continued. The symptoms became worse and on admission the patient was unable to walk. At this time she showed a slight pallor of the skin and mucous membranes.

The neurological examination revealed typical findings of posterolateral sclerosis.

The blood picture showed a hyperchromic anemia, hemoglobin, 74 per cent, red cells, 3,350,000. No free acid was present in the gastric contents.

Treatment with liver extract, intramuscularly, was instituted immediately. The response was satisfactory, both clinically and hematologically and upon discharge from the hospital one month later, the patient was able to walk with support. However, despite constant and adequate treatment during the past three and a half years, the patient is still unable to walk unaided, although requiring less support.

Case 4. (Adm. 379604) An Austrian housewife, aged 40, was admitted to the service of Dr. George Baehr in May 1935. For three years the patient had suffered with epigastric distress and vomiting. In March 1935 a nephrectomy for calculus

was performed, at which time the hemoglobin was 45 per cent. After this operation, progressive weakness ensued and walking became increasingly more difficult, until finally, for one week prior to admission, the patient was unable to get about. Examination showed a subicteric tint of the skin and sclerae and papillary atrophy at the edge of the tongue. The liver and spleen were palpable. The neurologic findings were typical of posterolateral sclerosis.

A severe macrocytic anemia was found, hemoglobin 45 per cent; red cells, 1,890,000. There was no free acid in the gastric contents.

Treatment with parenteral liver extract was instituted, resulting in prompt improvement. Upon discharge from the hospital the hemoglobin was 68 per cent and the patient was able to walk. During two years of treatment in the Out-Patient Department the patient was asymptomatic; however, treatment has been discontinued and the patient has not been seen for about ten months.

Case 5. (Adm. 388075) A Roumanian Jewess, aged 42, was admitted to the private service of Dr. J. H. Globus, December 1935. About a year previously the patient noticed coldness of the upper and lower extremities, which was soon followed by spasticity and weakness of the feet. Walking became uncertain and finally impossible. In addition incontinence of urine and feces developed. During this period the patient received a transfusion and ate whole liver, but without improvement.

Examination was negative, save for the neurological status, which was typical of subacute combined sclerosis.

Blood examination revealed a moderate macrocytic anemia with the hemoglobin 85 per cent and the red cells 3,200,000. No free hydrochloric acid was present in the stomach contents.

The patient was treated with parenteral liver extract which resulted in clinical improvement. Before discharge from the hospital the patient became continent and was not only able to leave the bed but to walk a few steps with assistance.

Case 6. (Adm. 397399) A German female, aged 60, was admitted to private service of Dr. C. Rabin in August 1936. For thirty years the patient had suffered from nausea, vomiting and meteorism. Her diet was greatly restricted and with the onset of menopause seven years before admission, there occurred headaches, increasing weakness, edema and loss of power in the lower extremities. These symptoms had increased in severity and during the four years prior to admission the patient was bed-ridden. In addition, paresthesias of the hands, dyspnea and palpitation had been present for two years.

Physical examination showed the patient to be emaciated with a yellow pallor. The liver was palpable. Neurologic findings were typical of advanced posterolateral sclerosis.

The blood picture was typical of pernicious anemia:—hemoglobin, 25 per cent; red cells, 810,000. There was also a gastric anacidity.

Administration of parenteral liver extract was followed by a favorable reticulocyte rise to 22 per cent and the blood picture improved progressively. At the same time there was a marked improvement in strength. Shortly before discharge, the patient was able to get out of bed and with support could stand and walk a few steps.

Case 7. (Adm. 405553) An Italian female aged 43, was admitted to the private service of Dr. D. Poll, March 8, 1937, complaining of increasing weakness, pallor and progressive loss of weight of six months' duration. Numbness of the hands and subsequently of the feet, as well as burning of the tongue, had also been noted. All the symptoms became aggravated in the two weeks prior to admission when the patient was unable to walk without assistance.

Examination revealed a marked lemon yellow pallor, atrophic tongue and a palpable spleen. The knee and ankle jerks could not be elicited. The Babinski sign was present on the left side. There was absence of vibratory sense in the lower extremities, but the position sense was intact.

Severe macrocytic anemia was present. Hemoglobin was 38 per cent and the red cells were 1,740,000. Achlorhydria was also present.

Treatment with parenteral liver extract was immediately instituted and following a reticulocyte rise of 15 per cent, the blood picture began to improve. Later the patient gained in strength and soon regained the ability to walk.

Case 8. (Adm. 415921) A German Jewish physician, aged 32, was admitted to the service of Dr. I. Strauss, in October 1937. Six months previously the patient had become aware of weakness and paresthesias of the hands followed by hyperesthesia of the legs, ataxia and increasing weakness, which finally resulted in his becoming bed-ridden. Neurological findings showed irregular pupils, bilateral hyperreflexia, a left Babinski; and a diminution of vibratory and position senses in the lower extremities.

Blood studies were diagnostic of pernicious anemia:—hemoglobin, 80 per cent; red cells, 2,940,000; color index, 1.3. Gastric contents showed no free hydrochloric acid.

Improvement in the clinical and hematological status followed the administration of parenteral liver extract. With returning strength the patient was soon able to walk. His blood picture became normal:—hemoglobin 98 per cent, red cells, 7,000,000. Since discharge bi-weekly injections of liver extract have been administered and he has showed a continued improvement.

Group II. Cases previously diagnosed as pernicious anemia with or without neuropathic involvement, who had developed paraplegia as a result of inadequate liver therapy or negligence in its continuance. Favorable response to liver extract.

Case 9. (Adm. 286410) A German housewife, aged 32, was admitted to the Service of Dr. Celler December 20, 1927 with a history of increasing weakness, palpitation and progressive pallor of three years' duration. There was marked improvement on a liver diet which had been carefully followed for about one and a half years. This treatment was discontinued and six months preceding admission the symptoms recurred with additional soreness of the tongue, progressive numbness of the feet, and finally inability to walk.

Upon examination the patient appeared slightly pale, there was an atrophy of the tongue and the spleen was palpable at the costal margin. Neurological examination revealed posterolateral sclerosis.

The blood picture was hyperchromic in type with a hemoglobin of 100 per cent and red cells, 4,320,000; color index, 1.1. Gastric contents showed no free acid.

The patient was started on a liquid liver extract, resulting in rapid gain in strength. The patient was at first able to stand and later walk with assistance just before discharge from the hospital. The gait, however, has remained ataxic and the neurological status remains unchanged despite constant treatment first with liver extract orally and during the past five years parenterally. The red cell count has remained between 3,800,000 and 4,200,000.

Case 10. (Adm. 295952) A Russian Jew, aged 39, was first admitted to the hospital in 1925 with a diagnosis of pernicious anemia. At that time the neurological status was negative. There was marked improvement after several transfusions.

In October 1928 the patient was readmitted to the service of Dr. B. S. Oppenheimer, suffering from extreme weakness, dyspnea on exertion and inability to walk.

Examination showed an atrophic glossitis, slight enlargement of the heart to the left, and râles at the bases of both lungs. There was a marked diminution of the position sense and loss of vibratory sense in the lower extremities. Absence of ankle jerks and some psychic instability was also noted.

The blood picture was typical of pernicious anemia:—hemoglobin, 69 per cent; red cells, 3,100,000; there was a gastric anacidity. During a month's observation liver extract was administered orally without any hematological response. However, there was some gain in strength and the patient was able to walk a few steps. The patient was then sent to a hospital for chronic diseases where death occurred one year later.

Case 11. (Adm. 370760). A German housewife, aged 56, was first seen in 1931 suffering from numbness of the toes and slight stiffness in walking. There was a minimum amount of neurologic involvement and a slight macrocytic anemia. The patient responded favorably to oral liver therapy which was continued irregularly for a year, during which time walking became increasingly more difficult. In July 1933, the patient was readmitted to the hospital with an acute cholecystitis. An operation was advised but refused. In November 1933 cholecystectomy was performed elsewhere and thereafter, for about ten months, liver therapy was neglected. In September 1934 the patient was readmitted to the hospital for the third time on the service of Dr. B. S. Oppenheimer. She complained of inability to walk for three months, numbness from the toes to the umbilicus, incontinence of urine and feces.

On the last admission patient presented a marked lemon yellow pallor and atrophic glossitis, a palpable liver and evidence of advanced subacute combined degeneration.

The hemoglobin was 37 per cent; red cells, 1,530,000.

Parenteral liver extract was immediately instituted, resulting in a prompt hematologic response, with a reticulocyte peak of 18 per cent. While in the hospital the patient became continent, but was unable to stand or walk upon discharge. During the past three years parenteral liver extract has been given regularly. One year after discharge the patient was able to sit up in a wheel chair and another year passed before a few steps could be taken with support. However, there has been steady improvement and at present with the use of crutches the patient not only is able to get about but to do her own housework as well.

Case 12. (Adm. 395912). An Irish housewife aged 48, was admitted to the service of Dr. G. Baehr in July 1936. Two years previously the patient had a severe anemia and an achylia, and was treated with liver and iron orally but did not respond to therapy. Since that time paresthesias of the fingers and toes developed with weakness and loss of power in the legs and partial incontinence of urine. The weakness of the legs increased progressively until finally walking became impossible.

The physical findings were essentially negative except for neuropathic involvement typical of subacute combined degeneration.

The blood picture showed a severe primary anemia with the hemoglobin 50 per cent and the red cells 2,130,000. There was an absolute achlorhydria.

Administration of parenteral liver therapy resulted in a favorable response. The patient was able to walk with assistance upon discharge from the hospital. The blood count on discharge was: hemoglobin, 71 per cent; red blood cells, 3,360,000. The patient remained on a maintenance dose of liver extract in the Out-Patient Department and continued to improve. After a time, however, therapy was discontinued and a typical relapse developed. Under the care of Dr. Peter Vogel adequate treatment has again been administered with resultant improvement.

Group III. Cases who failed to respond to liver extract; or refused adequate treatment

Case 13. (Adm. 302499). A 53 year old male was admitted to the service of Dr. I. Strauss in May 1929. Two years previously the patient suddenly developed spastic weakness of the lower extremities. Walking was difficult and this condition progressed until he was finally unable to get about. One week before admission difficulty in urinating developed.

The physical examination was essentially negative except for the neurologic findings of posterolateral sclerosis.

The blood count was typical of pernicious anemia with a hemoglobin of 80 per cent, and 3,800,000 red cells. The gastric contents showed no free hydrochloric acid. The urine showed albumin and pus.

Liver extract was given orally but the patient showed no improvement after six weeks of treatment. He was sent to a hospital for chronic diseases.

Case 14. (Adm. 382830). An Austrian male, aged 55, was seen on the service of Dr. George Baehr in May 1936. In 1916 a diagnosis of pernicious anemia had been made. The patient went into a spontaneous remission and remained well until 1926 when the symptoms recurred. He improved on liver diet and transfusion. For two years liver therapy was continued but in 1928 difficulty in walking was noted which gradually progressed. For the past six years the patient had been unable to walk. He had been taking liver at irregular intervals.

On the last admission he showed a lemon yellow pallor, a smooth atrophic tongue and a palpable liver. Neurological findings were those of marked posterolateral sclerosis. A marked macrocytic anemia was present; hemoglobin, 52 per cent; red cells, 2,350,000.

An absolute achlorhydria was found.

Treatment with parenteral liver extract resulted in prompt hematological and clinical response; after three weeks the hemoglobin rose to 75 per cent and the patient was able to sit out of bed and was just barely able to walk with assistance. Since discharge from the hospital, however, liver therapy has been discontinued. When last heard from he was only able to sit up.

Case 15. (Adm. 328453). A 54 year old woman was first admitted to the service of Dr. B. S. Oppenheimer in 1927 with a severe macrocytic anemia; hemoglobin was 25 per cent; red blood cells, 1,280,000; gastric contents contained no free acid.

There was a good response with liver extract given orally. The hemoglobin rose to 75 per cent; red cells to 3,450,000. For four years liver was taken regularly but in May 1931, the patient noted the appearance of a sore tongue, weakness in the upper extremities and an unsteady gait, all of which became progressively worse until there was complete inability to walk. On the last admission there was a generalized hyperreflexia, positive Babinski signs, loss of vibratory and position senses in the lower extremities. The blood picture showed a hyperchromic anemia; hemoglobin was 58 per cent; red cells, 2,650,000.

The patient was given increased amounts of liver extracts orally and after a week was discharged to a hospital for chronic diseases. No further improvement was noted as far as the paralytic status of the patient was concerned.

Case 16. (Adm. 318372). An American housewife, aged 37, was admitted to the service of Dr. I. Strauss in September 1930. Four years previously the diagnosis of pernicious anemia had been made and liver administered orally. This was taken irregularly and two years preceding admission the patient noted an increase in weakness and pain on walking, which became progressively worse. About a month

prior to hospitalization walking became impossible. During the year before admission lues were discovered and treatment instituted.

The examination was negative save for the neuropathic findings of subacute combined degeneration. In addition there were signs of a manic depressive psychosis.

The blood picture was hyperchromic, although the hemoglobin was 95 per cent and red cells, 4,400,000 with a color index of 1.1. Wassermann reaction was 3 plus.

Liver extract was administered orally but no improvement was noted during the two weeks the patient was observed.

Group IV. Paralytic cases who died before adequate treatment could be instituted.

Case 17. (Adm. 316686). An American housewife, aged 57, was admitted to the service of Dr. B. S. Oppenheimer in July 1930. She complained of marked mental depression, increasing stiffness and numbness of lower extremities and inability to move her legs, which conditions gradually progressed until the patient finally became bed-ridden. For three months prior to admission there was incontinence of urine.

Examination was negative except for findings of subacute combined sclerosis. The blood picture was hyperchromic and was as follows: hemoglobin, 86 per cent; red cells, 3,850,000. No free acid was present in the gastric contents.

Despite administration of liver extract orally the patient did poorly and there was no evidence of hematologic or neurologic improvement. A cystitis developed followed by a decubitus ulcer and septicemia. Death occurred one month after admission. Post mortem examination showed combined sclerosis.

Case 18. (Adm. 323873). A 67 year old housewife was observed on the service of Dr. I. Strauss in March 1931. The patient had been well until seven weeks before admission when, following an upper respiratory infection, increasing weakness developed in the lower extremities. This became worse until walking was impossible. In addition urinary difficulty was noted.

Examination. The heart was slightly enlarged to the left with a systolic murmur at the apex. There was a diminution of the knee and ankle jerks, absence of the abdominal reflexes, bilateral Babinski signs and absence of vibratory and position senses up to the waist.

The blood picture was typical of pernicious anemia, hemoglobin, 65 per cent; red cells, 2,350,000. There was an achylia gastrica.

Immediate oral liver therapy was instituted but before any response could be obtained death occurred. On post mortem examination funicular myelitis was found.

Case 19. (Adm. 400928) A Russian housewife, aged 62, was admitted to the service of Dr. George Baehr in November 1936, complaining of weakness and a sore tongue of three and a half years' duration. Because of blisters on the tongue and mucous membranes of the mouth, a diagnosis of pemphigus had been made and the patient had been treated with sodium arsenate. Progressive weakness had ensued, and four months before admission tingling of the hands and feet was noted. Rectal and bladder weakness developed and finally inability to walk. Upon examination the patient appeared chronically ill and had a lemon yellow pallor. The tongue was smooth and atrophic and the liver edge was palpable. The neuropathic findings were those of subacute combined degeneration.

There was a moderate hyperchromic anemia. Hemoglobin, 70 per cent; red blood cells, 3,530,000. The gastric contents showed no free acid after histamine. The sternal bone marrow was normoblastic.

A potent parenteral liver extract was administered to which the patient re-

sponded well, hematologically. The reticulocytes rose to 13 per cent on the eighth day and the hemoglobin to 80 per cent. However, the patient developed a decubitus ulcer with a subsequent septicemia and died one month after admission before neurological improvement occurred.

Case 20. (Adm. 416240) A Russian housewife, aged 60, was admitted to the service of Dr. B. S. Oppenheimer November 4, 1937. Six months before admission she suddenly became unable to walk and was forced to remain in bed. Marked weakness, anorexia and constipation developed in the intervening time.

Upon examination the patient appeared pale. There was slight atrophy of the papillae of the tongue; an indefinite slightly tender epigastric mass could be palpated. The neurological findings showed marked posterolateral sclerosis.

The blood picture on admission was typical of pernicious anemia. Hemoglobin, 44 per cent; red blood cells, 1,970,000; color index, 1.1. An absolute achlorhydria was present. Gastro-intestinal x-ray examination was suggestive of a gastric neoplasm but because of the patient's condition a satisfactory study could not be made.

Liver extract was administered parenterally and there was a reticulocyte response of 13.5 per cent. The blood picture improved remarkably, so that upon discharge the hemoglobin was 86 per cent; red cells, 3,700,000. During hospitalization the gain in strength was so marked that by the time of discharge, two and a half months later, the patient could move her legs and sit up in bed but walking was still impossible. The patient was sent to a hospital for chronic diseases where she died from coronary thrombosis.

COMMENT

These cases illustrate the most severe types of subacute combined degeneration observed in pernicious anemia. The paralytic manifestations indicate that the alterations of the spinal cord have reached an advanced stage of development. A study of such cases is important to prove the relative efficacy of liver therapy.

By the use of adequate and prolonged therapy with a potent parenteral liver extract the process was either arrested or improvement effected in most (Group I). Failures were due to some intercurrent infection or coronary thrombosis; such patients died before sufficient time had elapsed after the institution of treatment (Group IV). Many of the patients required long and persistent treatment, together with re-education of muscles or the use of orthopedic appliances, before they were able first to stand or walk with assistance and finally, in some cases to walk unaided. Others were more fortunate and were able to resume walking in a much shorter period.

The earlier cases were treated by the administration of whole liver or liver extract orally, whereas the later cases in the series received the parenteral form of extract. The response to oral administration was extremely slow; in Case I the anemia improved, but walking with assistance was impossible until about seven months after the institution of therapy. A few years subsequently the patient was able to walk with the aid of only an orthopedic appliance and crutches. The patients who received parenteral treatment usually responded more rapidly, as is illustrated by

Case 8 who, due to incorrect diagnosis, failed to receive liver extract for some time after the onset of symptoms. On admission to the hospital this man was unable to stand or walk, but after three weeks of intensive treatment standing was possible and later walking, without assistance. However, the response in Case 11 was extremely slow despite the use of potent liver extract and persistent treatment. The patient was bed-ridden for a full year before she could sit up in a wheel-chair, and now, after three years, is able to walk only short distances and must still use crutches.

In addition to the group of paralytics, there have been encountered in our series of 147 cases of pernicious anemia those with less marked neuropathic involvement, not sufficiently serious to render the patient bed-ridden, although some of the cases, due to debility from severe anemia, remained in bed. As soon as remission of symptoms occurred following treatment, these patients were able to stand and walk promptly without assistance. Of the 147 cases in the series, there were thirty-seven with mild symptoms of subacute degeneration and forty-eight with frank symptoms of neuropathic disease. Those with mild involvement presented such symptoms as soreness of the tongue, numbness and tingling of the hands and feet, and signs of slight reflex changes, slight loss of vibratory sense, and diminution in position sense. The frank cases presented more serious symptoms, including stiffness of the extremities, girdle sensations, difficulty in walking, and incontinence. Neurologically they presented more advanced involvement with hyperactive or absent deep reflexes, abnormal reflexes, positive Romberg sign and loss of vibratory and position sensibility.

It is of importance to note, also, that in forty-three, or 29 per cent of the cases, there were neither signs nor symptoms of any neuropathic involvement. Most of these patients have been adequately treated with liver diet and oral or parenteral liver extract. Some, however, have neglected therapy from time to time, and despite the resultant occurrence of one or more relapses during the period of observation, have, nevertheless, not developed any neural signs to date. Illustrative of this type of the disease are the following:

Case 21. (Adm. 400564) An American mechanic aged 42, was admitted to the service of Dr. B. S. Oppenheimer in 1929 complaining of persistent postprandial vomiting of six weeks' duration resulting in a loss of thirty-four pounds and progressive weakness and pallor. For one week prior to admission precordial pain, palpitation and extreme lethargy had been present.

Examination was entirely negative except for marked pallor, and there was no evidence of neuropathic involvement.

The blood picture was typical of pernicious anemia with hemoglobin, 35 per cent; red blood cells, 1,300,000. The gastric contents showed no free hydrochloride after histamine injection.

Liver extract orally was immediately administered resulting in a satisfactory response with a reticulocytosis of 19 per cent. At the time of discharge the hemo-

globin was 51 per cent and in the following months, while the patient was under supervision in the clinic, continued to improve. In July 1932 the patient discontinued liver therapy and within two months there was a recurrence of all original symptoms. When again seen in the hospital signs of severe anemia were present but no positive neuropathic involvement. After administration of parenteral liver extract, the blood picture returned to a normal level, where it has remained to date. The latest count was hemoglobin, 104 per cent; red blood cells, 5,600,000.

Case 22. (Adm. 291533) A Russian Jew, aged 62, first seen in June 1928 on the service of Dr. B. S. Oppenheimer, complained of increasing weakness, dyspnea and precordial oppression of three months' duration, with marked pallor and ankle edema.

Examination revealed a severe pallor, bilateral cataracts, emphysematous lungs. The liver was palpable. Neuropathic findings were negative.

The blood count showed a severe primary anemia with hemoglobin, 28 per cent; red blood cells, 1,070,000. There was an absolute achlorhydria.

Liver extract was administered orally with some clinical and hematological improvement. Upon discharge from the hospital the hemoglobin was 38 per cent and red cells, 1,700,000. The patient was observed in the Out-Patient Department and responded to liver therapy. After a time negligence produced a relapse which occurred in 1929, when liver extract orally again resulted in a fairly good response, the blood picture returning to normal. Another relapse developed in July 1932, again due to neglect of treatment, when the hemoglobin dropped to 49 per cent; red blood cells, 1,900,000. Once again resuming liver treatment, a prompt recovery ensued. A year later a mild relapse developed after stopping treatment. This time intramuscular liver extract was instituted with good results. For three years the patient received regular injections, but again after cessation of therapy another relapse occurred. In November 1937 liver extract was again resumed and the blood has returned to normal. At no time despite the repeated relapses have any subjective or objective neuropathic manifestations developed.

A number of patients observed for years, who have received continuous and adequate therapy with potent liver extract, have failed to establish a favorable hematologic response at any time. Despite persistently low blood counts, however, these patients have not developed signs of sub-acute combined degeneration. This aspect is illustrated by the following cases.

Case 23. (Adm. 343256) An American housewife, aged 62, was admitted to the service of Dr. B. S. Oppenheimer in January 1928. In the latter part of 1926 the patient had been treated at another hospital for precordial pain; a diagnosis of pernicious anemia had been made and a liver diet administered to which there was fair adherence, in the intervening year and a half. Seven weeks prior to admission, however, precordial pain, weakness and palpitation, again became manifest, together with a severe pallor.

Upon examination the patient had a lemon-yellow pallor and a cardiac murmur. There was no evidence of neuropathic involvement except for irregular pupils.

The blood picture was typical of pernicious anemia; hemoglobin, 20 per cent; red blood cells, 750,000. No free acid was present in the gastric contents after histamine stimulation.

The clinical response to liver extract orally was good and the blood count rose slowly to 45 per cent. Upon discharge from the hospital the patient was observed

in the Out-Patient Department and remained symptom free until July 1932, when upon discontinuation of liver therapy weakness promptly ensued accompanied by increasing pallor.

Upon readmission to the hospital the physical examination was similar to that on previous occasions, including the negative neuropathic findings. Hemoglobin was 25 per cent and the red cells, 950,000. Administration of parenteral liver extract induced a good response with a reticulocyte rise of 42 per cent; the count rose to hemoglobin, 42 per cent, while in the hospital and thereafter on regular liver therapy it reached 70 per cent. In the past six years the hemoglobin has rarely risen above that level and the red counts have never been more than 3,500,000. In spite of these low counts, however, there have never been any signs of neuropathic involvement.

Case 24. (Adm. 268032) A female school teacher has been observed from June 1926 to date. On the first admission to the hospital she was very weak and pallid and had lost a great deal of weight. There was a slight enlargement of the heart with a systolic murmur over the precordium and a palpable spleen. There was also absence of abdominal reflexes, ankle and knee jerks.

The anemia was typically hyperchromic and extreme in type; hemoglobin, 16 per cent; red cells, 440,000; color index, 1.8. No gastric analysis was made at this time, but on later observation achlorhydria was found.

The patient was given several transfusions with a good response. Upon discharge after a week in the hospital, blood count was 39 per cent; red blood cells, 1,770,000.

The patient was recalled to the Out-Patient Department where she was advised to eat whole liver, but was able to eat only about a half a pound twice a week. Her general condition improved and the blood picture improved slowly. The red cell count was less than 3,000,000, up to January 1929, and did not return to normal until October 1930. The patient discontinued liver therapy in February 1931 and a severe relapse occurred about a year later. She was then advised to take liver extract orally and the blood picture returned to normal; the blood picture was normal for the following three years, but another relapse occurred in September 1935 as a result of negligence. She was then given parenteral liver extract and since then her blood picture has been normal. It is remarkable that this patient had not complained of paresthesias or other neurological manifestations, despite the many relapses and the long duration of the periods of anemia.

DISCUSSION

Subacute combined degeneration may be considered one of the most serious complications of pernicious anemia. It is rarely encountered in other types of hyperchromic anemia, viz., sprue and achrestic anemia. For this reason it is imperative not only to make an early diagnosis of pernicious anemia, but to institute immediate and proper therapy in order to forestall the development or advancement of these neuropathic sequellae. This can be accomplished by proper study and interpretation of the blood picture in conjunction with demonstrating the presence of a gastric acidity after histamine stimulation. However, occasional cases of subacute combined degeneration may be observed without a blood picture typical of pernicious anemia and in such cases it is likewise important that liver therapy be promptly instituted.

Minot and Murphy (13) were among the first to emphasize the necessity of adequate treatment in pernicious anemia, with neuropathic involvement. Their criterion of satisfactory liver therapy is an erythrocyte level of five million, and they are of the opinion that at this level the cord symptoms are less likely to develop or progress. Allen (1), Connery and Goldwater (5), West (20) and others likewise insist that the red cell level must be maintained at this height for proper control of the disease. Goldhammer, Bethell, Isaacs and Sturgis (8) and Garvey, Levin and Guller (7) believe that a red cell level of over 4,000,000 may be considered indicative of sufficient therapy, whereas Schaller and Newman (15) and Mills (12) have observed that the red cell level was not of so much importance as long as regular potent liver is administered frequently and is varied from time to time to meet the needs of the patient. Needles (14) in studying our material, noted no progression of neuropathic signs in patients receiving liver extract regularly, even without a maximal hematological response.

The study of the effect of liver extract in the treatment of the paralytic type of pernicious anemia is also important because in this type of the disease the most dramatic improvements are to be observed.

If incontinence is present in these cases it is usually the first symptom to subside. Later the muscular tone improves and the patient as a rule is able to move the legs, though still unable to stand. After this the musculature of the back becomes stronger and sitting is possible. In some cases standing and walking follow shortly thereafter while in others many months may elapse before this is accomplished. Of the twenty cases in our series, eight did not make satisfactory progress. Of this number, four died within a few months after admission, and two were sent to other institutions because of marked mental symptoms. Another, though progressing well on discharge from the hospital, promptly discontinued therapy and now refuses liver in any form.

It may be noted that a more optimistic view has developed with respect to the paralytic type of pernicious anemia since the introduction of the parenteral liver extract therapy. In the early days many observers, especially Curschmann (6), Cohen (4), McAlpine (11) and Grinker and Kandel (9) believed that little improvement in the neurological picture followed oral treatment of these cases with liver extract. More recently, however, others have noticed marked improvement in some cases after liver therapy particularly, Minot and Murphy (13), Lottig (10), Bubert (3), Ungley and Suzman (19), Baker, Bancroft and Longcope (2). They reported that certain patients who had become bed-ridden due to advancement of the subacute combined degeneration were able to resume normal functions after intensive and prolonged liver treatment. These observations are confirmed in the present series. Failure to react is to be expected

in long neglected cases (Case 14) and in certain instances of an advanced type of the disease in which secondary infections are present.

In our experience, there appears to be no correlation between the duration of the paralytic symptoms and the time interval necessary for the restoration of function after active liver therapy has been instituted. Prompt response may be obtained in some cases who have been bed-ridden over a long period (Cases 6, 14), whereas, on the other hand, some patients with paralysis of a relatively short duration have taken the longest period for restitution of function (Cases 1, 11).

Successful treatment depends on the regular administration of liver or a potent liver extract, and repeated cautioning of the patient against negligence. The cooperation of the social service department of the hospital is essential for the control of dispensary patients. With such a procedure we have noted no recurrence or progression of serious neuropathic symptoms in cooperative patients, even though at all times the expected hematological response was not obtained. To some extent the latter may be discounted by the economic stringency of some of the patients which precipitated inadequate dietary regimes.

SUMMARY

(1) Of 147 hospital cases of pernicious anemia observed since 1928, twenty showed a paralytic form of neuropathic involvement.

(2) In the majority of these cases, prolonged and adequate liver extract therapy is most effective in arresting and retarding, improving, or preventing the aggravation of neuropathic symptoms.

(3) No recurrence or progression of symptoms of subacute combined degeneration occurred during administration of adequate treatment with liver or potent liver extract.

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THE EFFECT OF LARGE AMOUNTS OF LIPIODOL INJECTED INTO THE SPINAL SUBARACHNOID SPACE

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Sixteen years ago Sicard and Forestier (1) introduced the method of intraspinal injection of iodized poppy seed oil as an aid in the diagnosis of spinal cord tumors. They recommended the use of two to six cubic centimeters of lipiodol in the epidural space but advised the use of smaller amounts in the subarachnoid space. They stated that iodized oil should not be regarded as a permanent foreign body even if a long time is required for its absorption, and denied any tendency to cyst formation, such as that which follows the injection of mineral fats. In a few years, conflicting reports (2,3,4,5) appeared, based on clinical and experimental evidence. These reports described delayed inflammatory reactions after iodized oil injection, and a tendency to the formation of cysts containing the iodized oil. All observers have found immediate reactions in the form of an aseptic leptomeningitis which subsided in a few days. Sharpe and Peterson (6), Mac Laire (7), Bergerhoff (8), and others reported cases in which laminectomy was performed following the injection of iodized oil, and described inflammatory cysts containing the oil. However, in most of the above-mentioned cases, the neurological diagnoses were obscure, and the possibility of pre-existing arachnoiditis could not be excluded. It must also be remembered that in these earlier cases, as pointed out by Lindblom (9), the iodized oil may have undergone chemical changes before its use. Irritating free fatty acids and iodic fatty acids may have contributed to such inflammatory effects. Davis (10) and his co-workers objected to the diagnostic use of iodized oil on the basis of their experimental work in dogs. They injected one and one-half cubic centimeters of iodized oil into the subarachnoid space of ten dogs through a cisternal puncture. They found an inflammatory reaction of the leptomeninges, encysted globules of iodized oil, and pathological changes in the anterior horns and in the central canal of the cord. Their conclusions, however, are open to question. Preceding the injection of the iodized oil, they subjected their animals to laminectomy with the insertion of a rubber tube in the epidural space for the purpose of simulating a blocking lesion. Although they waited until the animals had recovered and showed no neurological signs, it is not improbable that some of their later findings were the results of the initial operative procedure.

Within recent years there has been an increasing interest in intervertebral disc and ligamentum flavum lesions as a cause of persistent low back pain (11,12). In order to accurately diagnose these lesions, the subarachnoid injection of large amounts of iodized oil was found to be necessary. The possibility of subsequent meningeal reaction and the non-absorption of the iodized oil have militated against the wider use of this method. In a comprehensive report, based on careful and repeated follow-up examinations of sixty-five patients, Globus (13) found no clinical evidences of irritative phenomena due to iodized oil, with the exception of one patient who had an accentuation of back pain. The period of

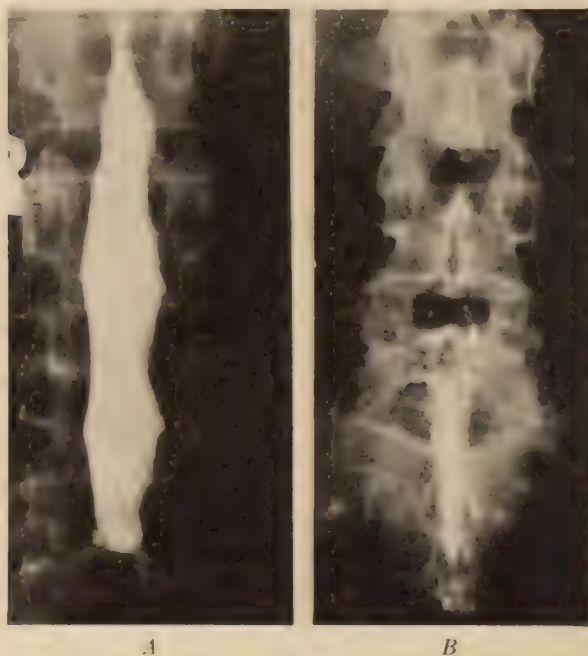


FIG. 1. *A.* After injection of five and one-half cubic centimeters of iodized oil. *B.* After removal of four cubic centimeters of iodized oil through a lumbar puncture.

observation extended from several months to four years, and in one instance to ten years after the injection. Three of his patients died, permitting a histological examination of the meninges, and no evidences of inflammation were found. The amounts injected were from one and one-half to two cubic centimeters, and occasionally a larger amount.

During the past year, eight patients in the hospital with low back disability, in whom intervertebral disc protrusions were suspected, had five to six cubic centimeters of iodized oil introduced into the subarachnoid space. When immediate fluoroscopic and X-ray examinations were

negative, an attempt was made to remove the oil in a manner suggested and previously carried out by Dr. L. Weinberger. The patient was placed in the lateral position with the shoulders elevated, and a lumbar puncture was performed at the dependent portion of the dural sac. Amounts ranging from one-half to four cubic centimeters were then removed by aspiration (Figures 1A and B). The total amount of iodized oil could not be withdrawn because of pain due to impingement of the lumbar puncture needle against the nerve roots.

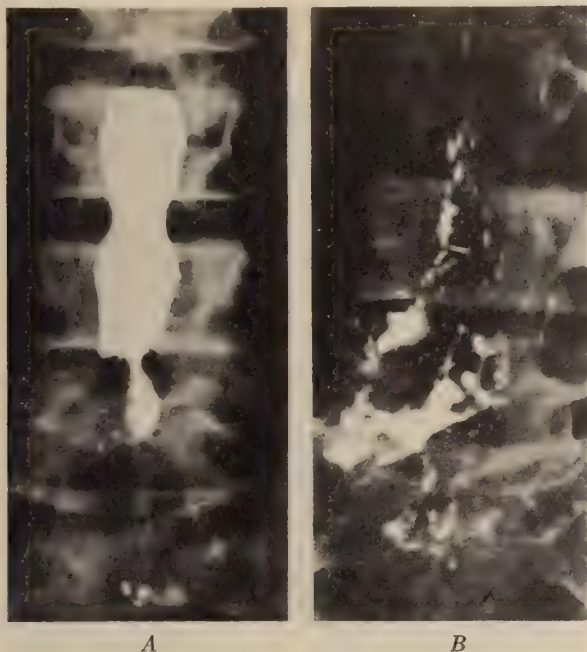


FIG. 2 (Case 1). A. Iodized oil shadow caused by prolapse of the fourth lumbar intervertebral disc (proved at laminectomy).

B. Amount of iodized oil remaining after laminectomy and removal of the prolapsed disc. The patient was symptom-free.

CASE REPORTS

Case 1 (Adm. 404206). A male, aged 58, presented the clinical features of a prolapse of the nucleus pulposus at the interspace between the fourth and fifth lumbar vertebrae. This was verified by lipiodolography. A laminectomy was performed by Dr. Ira Cohen, and the prolapsed disc was found and removed. This patient remained symptom-free, although an appreciable amount of the injected iodized oil was still present after laminectomy (Figures 2 A and B).

Case 2 (Adm. 406437). A female, aged 54, presented a less definite lipiodolographic picture of disc protrusion, but a laminectomy was performed by Dr. Ira Cohen. He noticed a bluish protrusion at the fourth lumbar nerve root on the right side and found it to be a large vein which he ligated. At operation, droplets of iodized oil

and an inflamed appearance of the nerve roots were noted. This patient has also obtained complete relief from her pain although a recent X-ray examination showed a large amount of oil still present after laminectomy (Figures 3 A and B).

Case 3 (Adm. 412955). A male, aged 52, stated that his back pain had become worse since the injection of lipiodol three months previously. Objectively, the right ankle jerk, which was diminished before the iodized oil injection, could no longer be obtained. However, X-ray studies of this patient showed a symmetrical persistent defect in the column of the iodized oil opposite the fourth lumbar interspace (Figure 4). Laminectomy was advised and refused. In this case, in which there was a partially obstructing lesion, there was no evidence of cyst formation and the iodized oil flowed freely.

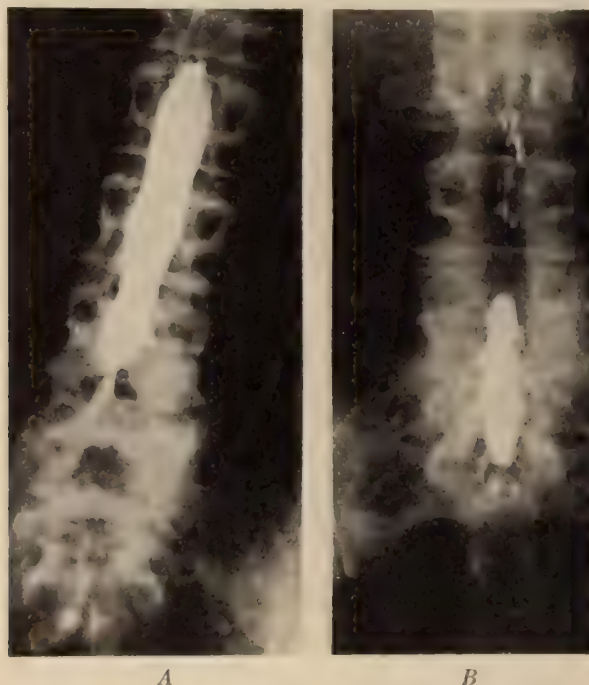


FIG. 3 (Case 2). A. Iodized oil shadow suggesting fourth lumbar disc prolapse. Not found at laminectomy.

B. Amount of iodized oil remaining after laminectomy. The patient was symptom-free.

Case 4 (Adm. 407255). A female, aged 34, had been very much improved since iodized oil injection, although only one-half cubic centimeter was recovered following a negative fluoroscopic examination. She also had a very severe immediate reaction. In her case a recent roentgenogram showed that the iodized oil had entered the sheaths of the thoracic and lumbar nerves to a greater extent than usual (Figure 5). Except for an inconstant area of hyperesthesia over the lateral aspect of the right thigh, no objective findings or subjective symptoms could be elicited.

In four other cases there were no objective or subjective signs which could be attributed to the iodized oil present in the subarachnoid sac. On fluoroscopic examination the main mass of oil could be seen to move freely, while smaller globules remained stationary in the nerve sheaths.

Every patient subjected to this test suffered an immediate reaction. Their temperature rose from 100°F. to 101°F., and there was usually an exacerbation of the pain in the back, radiating down the thighs. Some patients complained of headache, nausea, and vomiting. Two patients developed urinary retention which required catheterization for several



FIG. 4



FIG. 5

FIG. 4 (Case 3). Iodized oil defect suggesting disc prolapse or hypertrophied ligamentum flavum. This patient refused operation and stated that his pain was worse following the injection of iodized oil.

FIG. 5 (Case 4). Iodized oil in large amounts in thoracic and lumbar nerve sheaths. This patient was symptom-free.

days. The immediate reactions in the cases herein reported were more severe than in those studied by Globus. This was most likely due to the larger amounts of iodized oil used. Ebaugh and Mella (14) injected two cubic centimeters of iodized oil, and studied the spinal fluid of the thirteen patients so treated. They found that the cell count rose to 120 cells per cubic millimeter in twenty-four hours and fell to less than 20 cells per cubic millimeter in ninety-six hours. The spinal fluid protein rose to 130

milligrams per 100 cubic centimeters (normal 40 to 50) in twenty-four hours and persisted unchanged for ninety-six hours, after which no further chemical studies were made. They did not find any prolonged subjective complaints, nor were any objective findings noted. Forestier assumed that the intensity of the immediate reaction was directly proportional to the amount injected, but even after the use of five to six cubic centimeters he did not encounter any sphincteric disturbances. In this small series, two cases of urinary retention were found.

CONCLUSION

On the basis of the above observations (eight patients), it may be concluded that the use of large doses (five to six cubic centimeters) of iodized oil in subarachnoid injections, as a diagnostic measure when indicated, is without permanent deleterious effect.

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PSYCHIATRY AND THE CRIMINAL LAW

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In the past few years the subject of psychiatry and the criminal law has been the source of a great deal of discussion. The avalanche of material which has issued forth in the attempt to apply psychiatry to the administration of justice has produced bitter, unnecessary and, at times, even irrelevant controversy rather than understanding and progress.

The psychiatrist in presenting his point of view has occasionally overlooked some basic legal principles, and in attempting to clarify the problem has expounded his theories, using his vocabulary in such a manner as to confuse his opponent. The legal profession has presented its side similarly, and with equally confusing results. In some instances those interested in legislation, as well as in the functioning of criminal law, have actually resented the "intrusion" of the psychiatrist.

This result is not surprising, since by the very nature of their respective professions, the lawyer and the psychiatrist disagree in their conception of the etiological factors of human behavior. The difference between the two may be bridged if the whole question is reduced to simple premises, thereby making the controversy so pointed that it can be discussed in a much more direct manner.

For the purpose of elucidation, one must accept the premise that originally criminal law was based on the theory that man is a "free agent". This concept implied that all acts were willful and determined on a conscious level. From time to time modifications were made in the criminal code to include pathological cases, in which it appeared obvious that the particular criminal act was the result of a "diseased mind", rather than the conscious activity of a "free agent". The statute incorporating this medical diagnosis was formulated by the legal profession, and reached its final crystallization in 1843 in England.

It is now generally referred to as the McNaghten formula, and had its origin in the acquittal of one McNaghten on a charge of murder. The accused was a mentally ill individual, apparently suffering from paranoia. He was under the delusion that Sir Robert Peel was conspiring to harm him, and in order to "defend" himself he shot Peel's secretary, whom he mistook for the statesman. His acquittal brought about a popular demand for the revision of the law pertaining to insanity as a defense for a criminal act. An immediate investigation by the House of Lords resulted in the

passage of an act, that, "to establish a defense on the ground of insanity it must be clearly proved that, at the time of the committing of the act, the party accused was laboring under such a defect of reason from the disease of the mind, as not to know the nature and quality of the act he was doing, or, if he did know it, that he did not know he was doing what was wrong." This decision is at present the law in England and also in most of our States. Occasionally one finds some slight modification, but the basic principles remain as rigid as the first interpretation of almost a hundred years ago.

It is very interesting to note that the first real opposition to the McNaghten formula came from the legal profession, soon after this decision. A few judges in the United States attempted to reject the law, and far in advance of modern psychiatry, stated that there were other important factors to be considered. They wished to include the factor of irresistible impulse, thus raising the question as to whether or not the prisoner was a "free agent" at the moment in which the crime was committed.

A critical review of the application of the McNaghten formula to determine mental responsibility proves that it is impossible for the psychiatrist to function as an expert. A strict interpretation of the test for responsibility: "Did he know the nature and quality of the act and did he know it was wrong?" would make practically all individuals responsible for their actions, in spite of the fact that a medical diagnosis would indicate the presence of mental disease.

If we analyze the testimony given in numerous criminal cases we find, contrary to popular belief, a surprising agreement of experts in their presentation of medical evidence. A sharp, uncompromising difference of opinion arises when the psychiatrist, after giving professional testimony, is told to disregard his medical training and to apply an antiquated legal formula in order to determine the mental responsibility of the accused individual for the act in question. It is then that the psychiatrist is no longer able to function as an expert. No special medical or psychiatric training is necessary to answer the McNaghten formula as applied to the accused.

At times it appears that prosecutors, consciously or unconsciously recognizing some degree of mental illness in a prisoner, prepare their cases in such a manner as to make an obvious medical case appear normal under the rules of law. Recently a young man was arrested who had formerly been a patient of a State Hospital at which a definite diagnosis of a mental disease, progressive in nature, had been made. He confessed to the killing of two women and a man. In his recital of the sequence of events he stated that the man was killed last in order to prevent detection for the other killings. The motive for this last murder became therefore a rational one. This man was indicted, not for killing three people, but only for killing the one man. The McNaghten formula, as applied to the

act for which he was indicted might make of him a legally sane man, but could not alter the fact that he had been labeled by authorities of a State Hospital as suffering from an incurable, progressive mental disease.

Thus a situation is created whereby most individuals, legally committed by the court to State Institutions, may be released and certified as normal if the legal definitions used in criminal law are accepted as the criteria in determining mental illness. The advances made by psychology and psychiatry in the last fifty years make it impossible to accept the principles of law (determined in 1843) as they relate to human behavior and the interpretation of responsibility.

Some psychiatrists and legal authorities agree in refusing to accept the "right and wrong" test, and offer as an alternative the inclusion of a clause covering "irresistible impulse". This concept takes a more liberal view of the old theory that man is a "free agent".

A review of the history of this "clause" is interesting and relevant. In spite of the fact that in some quarters it is looked upon as something new, and perhaps ultra-modern, it is actually nearly a hundred years old, and was originally formulated by the legal minds of our American courts. The earliest recognition of the "irresistible impulse" had its origin in the courts of the United States as far back as 1834.

However, it was not until 1844 that an important decision was delivered, making use of this "yardstick" in determining mental responsibility for a criminal act. In discussing the defense of insanity, the chief justice in a Massachusetts Court stated in part: "In order to constitute a crime a person must have intelligence and capacity enough to have a criminal intent and purpose, and if his reason and mental powers are either so deficient that he has no will, no conscience or controlling mental power, or if, through the overwhelming violence of mental disease his intellectual power is for the time obliterated, he is not a responsible moral agent and is not punishable for criminal acts." He stated further in this very lengthy decision that: "if then it is proved to the satisfaction of the jury that the mind of the accused was in a diseased and unsound state, the question will be whether the disease existed to so high a degree that for the time being it overwhelmed the reason, conscience and judgment, and whether the prisoner, in committing the homicide, acted from an irresistible and uncontrollable impulse: if so, then the act was not the act of a voluntary agent but the involuntary act of the body without the concurrence of a mind directing it."

Some learned jurists have interpreted the phraseology of this decision as merely upholding the McNaghten formula. However, for many years the courts of about seventeen states, as well as the United States Supreme Court, have used this "test" in determining the question of "insanity" in criminal cases. Most psychiatrists, reading this decision, would agree in principle that it is a rather clear presentation of an acceptable method

of determining the presence of a psychosis in an individual accused of crime. In fact, in recent years, this formula has been accepted by some medical authorities as the solution of the whole problem. They have insisted that it offers a common basis for medico-legal cooperation. In a certain measure this is true, but they overlook the important inference that evidence of an irresistible impulse makes the individual "legally insane." This conclusion is just as untenable as the McNaghten formula. Whereas with that theory most men would be declared sane, the strict application of the irresistible impulse theory would make nearly all men "insane." The introduction of this provision does not take into consideration "irresistible impulse" as understood today and which is recognized as being present even in a "normal man."

The deterministic concept of present-day psychiatry is the basic cause of the conflict between law and medicine. This premise is at the root of all relevant controversy. The advances made in modern psychology and psychiatry, coming many years after legal formulations, contradict the premises on which laws have been constructed. This knowledge, by no means complete, clearly points to the conclusion that man is a product of his total past; that his behavior is an end-product conditioned by all that has gone before, and governed by conscious and unconscious factors. A criminal act is a form of behavior which can only be understood by the application of the foregoing theory. A confession of a crime relating clearly all circumstances pertaining to it, reveals only the conscious motives. The unconscious factors still remain unknown, although they are the basic motivating forces in the commission of an asocial act.

An essential function of law is to protect society. It is not enough to determine the guilt of a person charged with a particular crime; and either to sentence him to prison for a specific period of time or to acquit him because of irresponsibility for that act. Other factors of importance to be determined are the psychological forces at work in the person both in relation to the crime and to society in general, irrespective of the question "is he sane or insane?" One must remember that in the vast majority of cases the "criminal" is returned to society. A more effective security could be achieved if society had a better understanding of the criminal. Psychiatry can make a definite contribution to this phase of the question.

At the present time the hypotheses offered by psychiatry have not been actually incorporated into criminal law. Provision has been made to use psychiatry only as an aid to the judge or the jury in making their final decision. Until recently, if a plea of "insanity" was entered by a defendant the court was empowered to appoint a lunacy commission, consisting of three men, to determine this question. No provision was made by law to designate the personnel of the board but by practice the judges as a rule appointed a lawyer, a layman and a doctor of medicine. In rendering its decision the commission was bound by the McNaghten formula, and the court retained the power to accept or reject the findings.

Through the activity of Dr. Israel Strauss, as chairman of the Special Committee on Medical Jurisprudence of the New York Academy of Medicine, the most obvious defects have been corrected, by the enactment of two progressive laws. The first one establishes certain minimum standards for a qualified psychiatrist. The fact that this law was formulated by medical men and was sponsored by medical societies makes it ideal as well as practical. It will certainly have far-reaching effects in eliminating many of the abuses associated with the giving of expert testimony.

The second law gives the court, on its own motion or the motion of either the defendant or the prosecutor, the power to appoint a lunacy commission to determine the mental status of the prisoner charged with a felony. The law also makes it mandatory for the judge to appoint at least one qualified psychiatrist to serve on the commission. However the conclusions of the commission are still governed by the McNaghten formula, and the court still retains the prerogative of accepting or rejecting them: if it pursues the latter course the trial proceeds and the question must be determined by the jury. The presence of "insanity" is considered by law a question of fact and as such must be determined by the jury. It is not my purpose in this paper to discuss in detail the problem of putting a medical question, restricted in its presentation by rules of evidence, before twelve laymen. However, discussion with jurors reveals the confusion which exists in their minds as they listen to the medical testimony, thus proving that their findings are not actually based on the medical evidence.

Procedure in the conduct of a trial is such as to keep the profession of law intact. The jury of twelve laymen is charged to accept the law as interpreted by the court and to pass upon facts only. The medical profession is not given such an exalted position in the court room. Thus laymen are given the right to act as "psychiatrist-in-chief" to qualified medical authorities.

Roscoe Pound, when Dean of the Faculty of Harvard Law School, stated that dissatisfaction with the administration of justice is as old as law. As long as there have been laws and lawyers, conscientious men have believed that laws were but arbitrary technicalities, and that the attempt to govern the relations of men in accordance with them resulted in injustice. He defended law, or rather the rate of progress of law compared to that of public opinion, on the basis that law, of necessity, must lag behind, because it was formed by public opinion. Only when the latter has become fixed and accepted, can modifications in legal principles take place. He admitted that "free will" is a product, not a cause, of action, and what one takes to be reasons for actions are but rationalizations of what one desires to do.

Approximately fifteen years ago this learned exponent of law stated: "Within a generation psychology has risen to a practical science of the

first importance, with far-reaching applications on every side. Psychopathology has overturned much that the criminal law of the past had built upon. Indeed, the fundamental theory of orthodox criminal law has gone down before modern psychology and psychopathology. The results are only beginning to be felt. One result is a just dissatisfaction on the part of the medical profession with what they observe in judicial administration of justice and legal treatment of criminals But during the period of transition in which we are learning it and learning how to use it, there will be much experimenting and some fumbling and much dissatisfaction"

The statements made by this authority are a sufficient answer to those of the legal profession who have resisted the "intrusion" of the psychiatrist into the problem of criminal law. The great interest, on the part of the public, as well as the legislative bodies, in the subject of crime makes it possible today to bring psychiatry and law together. Many constructive suggestions have been made, but in the main, only one practical solution has been crystallized from the mass of material. The essential features of the plan have for their purpose the radical change of criminal law with regard to punishment. The criminal, "sane" or "insane," is considered a social problem. Public opinion is rapidly recognizing this fact.

Professor Salvador Mendoza, discussing the new System of Criminology in Mexico, stated: "The new Mexican Code abolishes the very word 'punishment.' It is inspired by the conception that society does not need to be angry and to be bitter against criminals in order to keep the welfare of the community. In drafting this new penal code we did not need to go, however, so far as to establish that all of the criminals are sick people, as some observers of the Mexican criminology have asserted. It was enough to assume that criminals are dangerous for the common interests of society for dealing with the problem. Nevertheless it seemed to us that society would have a better chance to combat the evil of crime, if it could acquire something like the coldness and simplicity of physicians and surgeons when they cut and cure."

Following these lines of thought, we come to the inevitable conclusion that there should be a practical plan which would eliminate the conflict of law and medicine and yet incorporate modern psychopathology in the administration of justice. Numerous suggestions have been made, but only one stands out and meets the conditions demanded by such a plan. The acceptable approach should be the elimination of the question of insanity or irresponsibility as a defense in a criminal trial. The individual accused of a crime should be tried only on the question of fact pertaining thereto. If on a factual basis he is found guilty, he should be sentenced to a "prison" which should be in reality a classification clinic.

The obvious conditions present prior to the trial, when guilt exists and truthful information is not attainable, are not conducive to a profitable

study of the mental makeup of the prisoner. It is only after trial, in such a classification clinic, that an ideal examination can be made and the results presented to a board consisting of, possibly, a lawyer, a psychiatrist, a sociologist and a criminologist. On the basis of their analyses and conclusions the length of sentence would be determined and the prisoner committed to an appropriate institution. No longer then will "the punishment fit the crime" but will "fit the criminal."

Only such a method can adequately clarify the whole problem and facilitate and make possible the protection of society against criminals who should never be returned to it. It affords as well the rehabilitation of those criminals who can, under certain conditions, be prepared to live in society.

This system deals directly with the criminal as the primary problem and with the crime as a manifestation of a symptom in a person unable to live according to the laws and customs of his community.

CONSERVATIVE SURGICAL CARE OF DIABETIC GANGRENE

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The number of patients with diabetes is increasing, and their life expectancy has been greatly lengthened by the introduction and use of insulin. In the majority of cases death is now the result of complications, rather than of the primary disease. By far the most important complication is the accelerated development of arteriosclerosis, which involves the cerebral, coronary and peripheral arteries. This process produces progressive impairment of circulation in the lower extremities and results in gangrene in many instances. During the past fifteen years diabetic gangrene of the extremities has become increasingly frequent, and more amputations are being done now than before the discovery of insulin. Satisfactory control of the diabetes by the use of insulin has made it possible for patients with this disease to reach the age period when gangrene of the foot is likely to take place.

Amputation of an extremity is more often required because of secondary infection than because of the gangrenous process alone. The loss of a toe, or several toes, due to gangrene is not, in itself, a disastrous event, and if the foot heals there is no serious interference with the patient's ability to walk. If infection could be prevented this outcome might be expected in the majority of cases. Secondary infection usually takes place at the junction of the necrotic and living tissue, and spreads from this point along tendon sheaths or tissue planes. Once this has happened, the entire outlook for saving the extremity is changed. Attempts to drain the infection by incisions result in still more gangrene and frequently are unsuccessful in preventing further spread. Rapidly ascending lymphangitis, high temperature, marked insulin resistance and evidence of general toxemia then make amputation necessary in order to save life.

The most important problem in the care of diabetic gangrene is the maintenance of the sterility of the gangrenous zone until the necrotic tissue has separated, and the resulting wound has completely healed. When gangrene develops in a patient with diabetes, it is usually at the tip of a toe and it is dry and uninfected (Figure 1). If such a patient is immediately put at rest and if the sterility of the gangrenous area is scrupulously maintained, there is a fair likelihood that the gangrenous process will limit itself to the toe (Figure 2), that it will separate in a period of a few weeks, and that the wound will slowly heal (Figures 3 and 4). It is my practice to maintain sterility of the gangrenous area by painting the

entire foot with five per cent picric acid in alcohol, and applying a sterile dressing up to the ankle. Sterile gauze is placed between the toes to avoid pressure of one toe upon another. Whenever this dressing is removed, for purposes of cleanliness the foot is again completely painted with picric acid and a new sterile dressing applied.

In addition to the local care of the foot, the diabetes must receive attention. It is the experience of surgeons that glycosuria is disastrous in the presence of gangrene or infection. Proper control of the diabetes from the



FIG. 1. Uncomplicated diabetic gangrene showing involvement of the tips of the toes.

surgical standpoint means a complete absence of sugar in the urine. A moderately elevated blood sugar in the absence of glycosuria does not appear to cause any trouble. Regulation of the diet and reinforcement of the patient's ability to utilize carbohydrates by insulin are essential for the proper care of the surgical diabetic. If the sterility of the area of gangrene can be maintained and glycosuria can be avoided, the prognosis for saving the extremity is excellent.

Measures to increase the circulation in the extremity should be employed. These may include the administration of vasodilator drugs, the



FIG. 2. Diabetic gangrene of the great toe showing tendency to demarcation at the base of the toe.

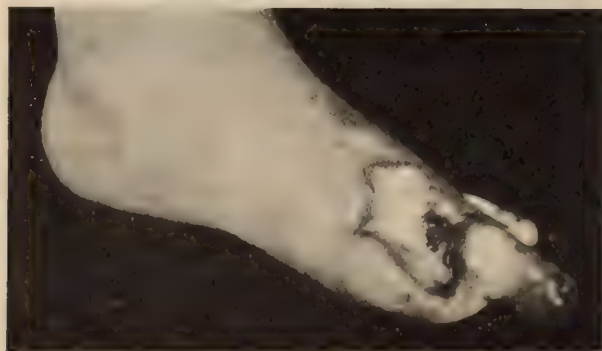


FIG. 3. Satisfactory healing following spontaneous loss of the great toe, due to diabetic gangrene.

free use of alcohol by mouth, the intelligent application of heat, the use of postural exercises and of mechanical appliances to aid the circulation.

Heat properly used is often of value, but if improperly applied may result in disaster. The devitalized tissues of the lower half of the leg and foot will not tolerate a degree of heat which could be applied to a normal extremity without harm. The unregulated baking cradle placed over the affected foot frequently results in a marked increase of pain and the development of an extensive burn. Rapid spread of the gangrene is likely



FIG. 4. Complete healing of foot following diabetic gangrene of all toes

to take place as a result of such unwise use of heat. Heat is applied in order to produce reflex peripheral vasodilatation. It is therefore better applied to some portion of the body other than the affected extremity. It is a safe rule that excessive heat should never be used below the middle of the calf. The thermo-regulated cradle, in which a temperature no higher than 95 degrees F. is maintained, may safely be placed over the affected foot. The use of heat at this temperature will not produce a burn and often adds to the patient's comfort.

If the gangrenous area becomes infected, the entire outlook is changed. The primary objective of treatment must be to control infection, for as long as this remains active it is difficult to prevent spreading of the gangrene and almost impossible to properly control the diabetes. The three cardinal signs of uncontrolled infection are elevation of temperature, increased insulin resistance and lymphangitis. Incision and drainage of localized collections of pus must be performed without delay and with minimum trauma to the devitalized tissues of the foot. A dressing of gauze, soaked in 50 per cent alcohol or in a solution of equal parts of alcohol and 50 per cent boric acid solution, is often of assistance in controlling infection. Soaking the foot for ten minutes, twice a day, in a bath of Carrel-Dakin solution, of boric acid solution, or potassium permanganate solution may also be of value. Success in treatment is indicated by a fall in temperature, disappearance of the lymphangitis, and disappearance of insulin resistance. Infection in a diabetic foot is always grave and the seriousness of the condition is not much minimized even by a fair circulation. In general, it may be said that if the infection is limited to the dorsum of the foot the prognosis is still favorable, while if it involves the plantar surface of the foot the prognosis is unfavorable, because of the greater number of tissue planes in which infection can spread. In spite of adequate incision and drainage of an infected focus, there is always a great tendency for infection to spread further beyond the limits of the incision. Each time the incision is extended, the infection spreads still further and ultimately proves uncontrollable. When a patient with a diabetic gangrene develops secondary infection, the outlook for saving the extremity in most instances is poor. The best treatment is prophylaxis against this exceedingly unfortunate and preventable complication. This is particularly the responsibility of the family physician, for he sees the patient when the gangrenous process first develops. Since most of the patients with diabetic gangrene already have secondary infection when they are admitted to the hospital, it is obvious that the family physician is not meeting this responsibility.

When the loss of the extremity becomes unavoidable, the level at which amputation is to be done should receive careful consideration. When extensive gangrene is present in a diabetic, it is a valid assumption that there is serious impairment of circulation in the extremity. It has been taught for many years that amputation should be done through the thigh in order to insure adequate circulation for healing. The mortality following thigh amputation for diabetic gangrene ranges from 35 to 75 per cent (Table I). During the past eleven years sixty-eight mid-thigh amputations for this condition have been done in the wards of The Mount Sinai Hospital with a mortality of 38 per cent. An analysis of the mortality shows no improvement in recent years (Table II). The percentage of deaths in 1933 was 42 per cent; in 1934, 57 per cent and in 1935, 50 per

cent. Circulatory complications, such as shock, cardiac failure, and cerebral and pulmonary embolism, were responsible for nine of the twenty-six deaths. Toxemia and sepsis, secondary to gross infection of the stump,

TABLE I

Mortality Following Amputations for Diabetic Gangrene in Various Hospitals

HOSPITAL	REPORTED BY	WARD OR PRI- VATE	NO. OF CASES	YEARS	PERCENTAGE OF MORTALITY
Philadelphia General.....	Eliason (5)	Ward	130	1926-1933	56
Philadelphia Episcopal.....	Crossan (4)	Ward	56	1926-1935	50
Mary Immaculate (Jamaica)...	Levin & Dealy (6)	Ward	25	1930-1935	50
Montefiore.....		Ward	17	1932-1936	59
Massachusetts General.....	Kuhns & Wilson (7)	Ward	36	1916-1926	33
Mount Sinai.....		Ward	68	1926-1936	38
Morrisania.....	Williams & O'Kane (8)	Ward	65	1931-1935	60*
Bellevue, first division.....	Lee, John Gordon†	Ward	40	1931-1935	52
Bellevue, second division.....	Miscall, Laurence†	Ward	35	1931-1935	63
Bellevue, third division.....	Standard, Samuel†	Ward	70	1931-1935	37
Bellevue, fourth division.....	Samuels, Saul†	Ward	24	1931-1935	75
New England Deaconess.....	McKittrick & Root (9)		72	1923-1927	18

* Average mortality for 5 years.

† Reported at Academy of Medicine May 11, 1937.

TABLE II

Analysis of Mortality Following Mid-Thigh Amputations for Diabetic Gangrene and Infection in Ward Cases at The Mount Sinai Hospital (1926-1936)

	NO.	LIVED	DIED	PER CENT
1926	3	1	2	66
1927	8	5	3	35
1928	7	3	4	57
1929	2	2	0	0
1930	6	6	0	0
1931	4	3	1	25
1932	6	5	1	17
1933	12	7	5	42
1934	7	3	4	57
1935	10	5	5	50
1936	3	2	1	33
Total.....	68	42 (or 62%)	26 (or 38%)	

accounted for fourteen deaths (Table III). An average mortality of 50 per cent for a relatively simple operation indicates that mid-thigh amputations are beyond the endurance of most patients with diabetic gangrene.

It is possible that the shock and fall in blood pressure which results from cutting across the muscles of the thigh and from treatment of such an extensive wound play an important rôle in producing the secondary thromboses in coronary and cerebral vessels. The fall in blood pressure during anesthesia with ether, or during spinal anesthesia, may also be a contributing cause. In any case, it is poor surgical judgment to continue to carry out an operative procedure which is beyond the strength of the patient.

A second consideration is the frequency of infection in the stumps of thigh amputations. Thirteen of the twenty-six deaths are attributed to toxemia and sepsis secondary to such infection. The assumption is warranted that in most of the patients amputation carried out at the level

TABLE III

Cause of Death in 26 Patients Who Died after Mid-thigh Amputation for Diabetic Gangrene

Shock.....	3
Toxemia and Sepsis.....	14
Cardiac Failure.....	3
Pneumonia.....	3
Pulmonary Embolism.....	2
Cerebral Thrombosis.....	1
Total.....	26

TABLE IV

Treatment of Stump and Number of Infections*

Primary closure.....	22	Infected.....	12
Left open with closure 2 days later	11	Infected.....	5
Left open	25	Infected.....	22
	58	Infected.....	39

* Ten patients who died in the first few days postoperatively are excluded.

of the mid-thigh was done through uninfected tissues. In spite of this fact, 70 per cent of amputations done at this level resulted in grossly infected stumps (Table IV). Primary closure was tried in twenty-two cases and twelve of these became infected. In eleven cases the muscles were loosely sutured over the bone and the superficial wound was packed with iodoform gauze. If no necrosis of the skin flaps or infection of the stump was present in forty-eight to seventy-two hours, secondary closure was carried out. Five of the eleven cases treated in this manner subsequently showed signs of infection and the stump had to be re-opened widely. In twenty-five instances no attempt was made to close the stump, and twenty-two of these were infected. Apparently the patient with diabetes is unable to overcome infection, as the non-diabetic is able to do.

Even the minimal infection which takes place during the operative procedure readily obtains a foothold, and in a short while gross infection of the stump results. Various attempts to meet this problem by primary Dakinization of the stump or by packing the wound with gauze soaked in alcohol have failed to solve the problem.

The widespread belief that thigh amputation is necessary to insure adequate healing has been proved incorrect by numerous surgeons in the past few years. McKittrick (1), Beverly Smith (2), Maes (3), Crossan (4) and others have advocated amputations below the knee, and have reported good results following this procedure. My own experience also indicates that amputations can be safely performed below the knee in diabetic patients, even though the popliteal artery is closed and oscillometer readings indicate a seriously deficient circulation.

The advantages of amputation below the knee are threefold: lowered operative mortality, improved function, and less psychic shock. Although my present series of cases is small, the indication is clear that a considerable reduction in operative mortality can be expected following amputations below the knee. The use of an artificial limb is greatly facilitated if the patient retains his knee joint and about six to eight inches of his leg. Such patients are able to walk without the use of a cane or crutches, and with scarcely any perceptible limp. Finally, for the average patient, the loss of the extremity through the midleg causes much less emotional disturbance than an amputation through the thigh.

The patient with diabetic gangrene is usually a poor operative risk. He is past middle age, and often has complicating arteriosclerotic cardiorenal or cerebrovascular disease. His vitality has been reduced by prolonged suffering and by absorption of toxic products from his gangrenous or infected foot. To relieve pain he has been given considerable quantities of narcotic drugs. It has been difficult to properly control the diabetes because of the diminished effectiveness of insulin in the presence of infection and gangrene. Good judgment dictates that such a patient should be subjected to as little operative trauma as possible. To accomplish this purpose the operative procedure should be brief, profound anesthesia should be avoided, and amputation should be carried out as far distally as possible. The operation should be divided into two short stages, rather than one long one.

The reasons for subjecting these patients to the discomfort of a two stage operation must be briefly stated. The primary objective of an amputation for diabetic gangrene is to rid the patient of a gangrenous or infected foot which threatens his life. Surgery of this character is essentially emergency in nature, and must be done regardless of the poor condition of the patient, improper control of the diabetes and unfavorable operative conditions. From the standpoint of its value as a life-saving procedure, it matters little whether the initial stump obtained is a satisfactory stump,

and it would be poor judgment to endanger the attainment of the primary objective in order to accomplish a secondary one. To fashion a satisfactory stump, the bones must be divided at a higher level than the skin. This requires additional time and considerable invasion of tissue planes. In the presence of lymphangitis, secondary infection in these tissue planes



FIG. 5. Well healed amputation stump below the knee following two stage amputation for diabetic gangrene.

is very likely to occur, and thus the patient is not rid of the disease which threatens his life. These are valid objections to an attempt to obtain a satisfactory stump at the primary operation.

My procedure is as follows: At the first operation a guillotine amputation is done a few inches above the ankle. The bone is cut across at the

same level as the skin and no attempt is made at this stage to obtain a satisfactory stump for later use. The operation is done under gas-oxygen anesthesia, no tourniquet is used, and the procedure requires less than five minutes. There has been no mortality following this primary procedure. Following this operation the severe pain which originated in the foot is at once relieved and the diabetes can readily be brought under control. Patients are allowed out of bed on the day following the operation and very soon may be allowed to use crutches.

After a variable period of time, usually two to four weeks, a secondary plastic operation is done in order to obtain a satisfactory stump. By the time the second operation is undertaken the patient is in good condition, his diabetes is well controlled, his general condition is much improved by elimination of the necessity for narcotics, and the stump presents a healthy granulating wound. After careful preparation of the skin and sterilization of the wound, anterior and posterior flaps are made a few inches above the site of the primary guillotine operation. The bones are resected, the wound is packed or drained and the flaps are allowed to fall together. After two or three days, if the wound remains clean, the gauze is removed and the flaps are approximated with adhesive strapping (Figure 5).

As might be anticipated, there have been a few failures in carrying out this method. In two instances attempts to obtain rapid healing by primary closure of the stump after the second stage operation resulted in infected wounds. One of these patients died of the infection; the other survived a mid-thigh amputation. In one instance necrosis of the skin developed after the primary operation, and a mid-thigh amputation was necessary. Such failures may be attributed to inexperience with a new method, and they may be avoided by altering the technique or by selecting the cases more carefully.

SUMMARY AND CONCLUSIONS

1. Uncomplicated diabetic gangrene develops at the tips of the toes and is often limited to one toe.
2. Secondary infection of gangrenous areas is preventable.
3. If the sterility of the gangrenous zone is maintained the prognosis is good.
4. When gangrene becomes infected the prognosis for saving the extremity is poor.
5. The cardinal signs of uncontrolled diabetic infection are elevation of temperature, increased insulin resistance and lymphangitis.
6. Amputations are more often required for spreading infection than for gangrene.
7. Amputation in two stages below the knee is recommended, and the technique and the reasons for this procedure are discussed.

I wish to thank Doctors Lewisohn, Beer, Neuhoi, and Colp for permission to study and report the statistics of amputations in diabetic patients on their services.

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RATIONALE AND PSYCHOTHERAPEUTIC METHODS OF THE VOLUNTARY MENTAL HOSPITAL

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The provision of adequate psychiatric facilities is an eternal triangle and affords more complicated predicaments than a problem play. The three elements essential to effective functioning of such facilities are: 1) professional awareness of what type of care is required (on the part of psychiatrists); 2) community conviction that will provide funds to have the plan carried out; 3) education of that part of the public which requires the type of care offered.

Two decades ago the objective of the mental hygiene movement was to develop more extensive facilities for the care of psychiatric problems and simultaneously to educate the public as to the necessity for the early treatment of mental disorders. It was at this time that the Jewish Mental Health Society was organized for the purpose of developing and maintaining psychiatric clinics. While engaged in this work, the sponsors became increasingly cognizant of the large number of patients who could not be treated effectively at the out-patient clinics and who at the same time were not suitable cases for a state hospital. Among those patients were the ones who needed removal from their environment as part of the treatment plan and also those the severity of whose illness required more intensive psychotherapy than the clinics were equipped to give.

The mere establishment of a special institution for the treatment of borderline mental disorders would not solve the problem. People suffering from such disorders had a morbid fear of hospitalization, and an institution of this type had to set for itself a program of disabusing its potential patients and the community of the prevailing idea that such hospitalization is synonymous with stigma or disgrace.

Dr. Israel Strauss, the President of the Jewish Mental Health Society, who was responsible for the establishment of psychiatric clinics which subsequently were taken over by the respective hospitals when their success was proved, now conceived the idea that the establishment of an institution particularly adapted to the treatment of borderline disorders was an essential link in a planned psychiatric program. It was believed that borderline mental patients, successfully treated in a hospital of this type, would become potent instruments in creating an enlightened attitude toward mental hospitals on the part of the public and in overcoming

the fear of hospitalization that impelled so many sick people to run aimlessly from clinic to clinic and from physician to physician.

As a result of Dr. Strauss' unremitting efforts, an institution of this type was established. The name chosen, general in character, included the term "hospital" for the purpose of informing the public that active treatment was offered. Suitable patients were to be admitted irrespective of their ability to pay, though those who were in a financial position to pay, in part or in full, for their care were required to do so. Admission was open to borderline mental patients and severe psychoneurotics who were willing to come voluntarily, i.e., those people who had an awareness of their illness and desired treatment. It is a fact that no person can receive extramural therapy in any form unless he is ready to accept it, and it was believed that the same approach should be used in the hospital. Experience has confirmed the validity of this approach. We find that when a patient knows he can be discharged from a mental hospital as readily as from a general hospital or from the care of a private physician, his acceptance of treatment is more assured and he seldom leaves the hospital until the time is ripe for his discharge. On the other hand, it has also been our experience that the patients who leave the hospital before their treatment is completed are usually those who have been induced to come by friends or relatives; these are generally the patients whom we find unsuitable for psychotherapy and whom we are prepared to discharge before treatment is instituted.

Before discussing hospitalization, it becomes necessary to state that economic factors are the prime consideration in determining whether the vast majority of borderline cases are to be treated extramurally or intramurally. We are fully aware that a great many patients can be treated extramurally, provided they can be removed from home, placed under the supervision of a good psychiatric nurse and receive adequate treatment from a psychiatrist. Such plans, however, are not feasible for the vast majority of patients who cannot meet the cost.

It would be futile to go into a classification of which disorders should be hospitalized and which should be treated extramurally. Experience has strengthened our conviction that the psychoneuroses and the mild mental cases, when removed from their environment early enough and placed under the proper therapy, can be cured much more rapidly and thoroughly than when they remain at home. While it is hard to generalize about cases that should be hospitalized and those which should not, some guiding principles seem justifiable. We hold the belief that those people who can no longer cope with their economic and social responsibilities and who take too heavy a toll from those close to them should be hospitalized. This applies equally to the head of the family who is no longer able to go on with his employment or his business and seriously disrupts the emotional equilibrium of his family, to the housewife who can no longer manage her

children satisfactorily and who menaces her husband's ability to carry on his end of the responsibility, or to the young person whose demands on his family are so great as to encroach significantly on the rights of his siblings. On the other hand, those people who remain socially intact and tolerably self-reliant economically, even if it is at great cost to themselves, should be treated outside a hospital. This would explain why some anxiety neuroses can be treated on the outside while others require hospitalization. In other words, when an obsessional-compulsive neurotic can control his anxiety and his obsessions to the extent that he is able to continue with the more important pursuits, every effort should be made to adjust him on the outside. When the obsessions and his worry over them become an insurmountable obstacle to his making a living or his participating in a social group, hospitalization becomes essential. In the field of depressions, considerations of economic adequacy are no longer paramount: even if the depression appears mild and there are apparently no suicidal ideas or threats, hospitalization is essential as a safeguard. In dealing with adolescents of schizoid character, it is our opinion that if these individuals are sufficiently in contact with reality to pursue their schooling or their occupations, every effort should be made to adjust them on the outside, to avert further retreat from reality.

The only groups for whom hospitalization is definitely contraindicated are those who manifest symptoms of a narcissistic trend and chronic neurasthenics. These people may get themselves acclimated to the new environment and remain completely contented, without making any effort to improve. There is grave danger of prolonging the illness by the injudicious institutionalization of such patients because the hospital acts as a shelter from reality.

In general, it is our belief that the psychoneuroses and mild psychoses—except for those for whom hospital care is contraindicated—benefit by their removal to a hospital. This belief that removal from their home environment is in itself a therapeutic measure is confirmed by our observation of numerous patients who, upon admission to the hospital, have shown a sudden improvement. We have, therefore, been forced to the conclusion that the improvement was due to the change of environment and could not be attributed to the disease having run its course and having incidentally terminated in hospital surroundings. To emphasize this point, we can cite many cases in which the family, encouraged by the sudden improvement, removed the patient before ego organization was achieved, with a consequent reappearance of the original picture. While it is undeniable that many of these patients' subsequent difficulties are traceable to early trauma and repressed infantile difficulties, it is equally pertinent that the crystallization of their illness is precipitated by emotional stress and certain strains in their present environment. Something of an exogenous nature obviously stimulates the onset of the disorder and

since this etiological factor arises in the environment, early removal from this irritation is essential. Where such removal does not take place early, the pathological psychic pattern becomes firmly established, treatment presents additional difficulties and recovery is delayed.

The rôle played by the patient's home environment in augmenting his illness can be appreciated best when one lives with these patients daily and observes their reactions to visiting days. The great majority of patients not only react adversely to the actual visits but show marked effects on the day preceding such visits and on the following day. One may dismiss the problem by attributing their difficulties to homesickness, but if one listens to their conversations and observes their behavior, one notes that the patient pours forth an accumulation of symptoms to the family. Whether it is the patient's sense of guilt, an expression of punishment, or his effort to justify a longer hospitalization, is a problem which requires considerable analytic study. Our point is that for the purpose of practical treatment, this behavior points to the necessity of removing the patient from the environment.

When we place stress on removal from the patient's former environment, we have in mind several conditions that are essential to making such a change a positive experience. The most important of these, of course, is that the change to the hospital has to be the patient's own choice. This condition, in turn, presupposes that the patient has at least a realization that he is mentally ill, and a desire to receive treatment for his condition. Before his admission, it is essential that he understand that if the hospital does not come up to his expectations, he can be discharged readily. An important feature for him to understand is that the other patients at the hospital are on a similar voluntary status and that the hospital does not accept patients whose condition is so severe as to make them incapable of making their own choice or decision. This immediately disabuses the patient of any preconceived notions as to "insanity" or being hospitalized among "madmen." The patient also receives some encouragement from the explanation that the hospital does not accept "incurable" cases and that his acceptance means that at least on superficial observation it is believed that something can be done for him.

Upon the patient's admission, the nature and conduct of his first interview with his physician will play an important rôle in his subsequent treatment. To gain the patient's cooperation and confidence, it is essential to make the first interview as pleasant as possible, to put the patient at ease and to relieve his anxiety or fear about the "unknown." The patient is given as much time as he wants to elaborate his difficulties. The routine of the hospital is explained to him and an effort is made to explain to him how the hospital attempts to treat such problems. Thus a rapport can be established between the patient and the physician which will make it easier for the patient to approach the physician again. This is

analogous to the situation in which the patient, brought to a general hospital for an operation is in a state of anxiety because, not knowing the operating surgeon, he fears what will happen to him. It is well recognized that there is much less panic when the patient knows his family doctor will be there or when he knows the surgeon's reputation and has met him.

The actual treatment at the hospital is eclectic in character. The term "eclectic" is sometimes used as an evasion, or to justify the absence of a definite philosophy. It is our conviction that effective therapy demands a critical evaluation of existing schools and their methods, and that loyalty or adherence to a particular school of psychiatry is frequently inimical to such intellectual freedom. As a matter of fact, the history of psychotherapy is punctuated by dogma. Each progressive step, every new concept or discovery which had its forceful adherents, was anathemized, then accepted and subsequently, in turn, became a barrier to further progress. Without going back too far, all we have to think of is the war over the cessation of mechanical restraint, the advocacy of chemical restraint and then its complete rejection; first complete resistance to Freudian psychoanalysis and then its unqualified acceptance. Methods and schools of thought, instead of being regarded as sign-posts, become creeds, and both adherence and denial are accompanied by religious fervour. The fact remains that we cannot afford such high-handedness, if only because the treatment of the mentally ill is still chiefly an art based on a scientific foundation. We cannot disregard the fact that we have by no means arrived at an understanding of the real etiology of mental disease. We have shifted completely from the purely organic viewpoint to the functional—so completely that treatment itself has become pigeon-holed into theories of behavior. The fact that we do not find any gross pathology in the disease entities of the neuroses and psychoses (using "disease entity" in a medical sense) does not remove these diseases from the sphere of disturbed functions of the brain and its appendices. Recent treatment of dementia praecox with hypoglycemic shock and metrazol begins to indicate that this disturbance is not entirely a psychic deviation and that there is probably a bio-chemical imbalance producing the disorder.

Without entering into a discussion of the minor adjuvants of treatment, such as occupational therapy, recreation, the stimulation of outside interests, etc., which require intelligent direction, we would like to discuss certain phases of treatment which are more debatable. One of these is the use of drugs. The administration of these was until recently held in disrepute, and it was the proud boast of hospitals that they "used no drugs." Bearing in mind that patients come to a hospital in a state of anxiety and panic which actually produces physical distress and an accentuation of their anxiety, we recommend that these conditions be relieved by the judicious use of proper medication. This is not a recommendation of medication versus psychotherapy. A sedative allaying the general

tension or confusion has in a great many instances helped to clear up conditions by putting the patient in a state receptive to other forms of therapy. In the acute panics in which a psychotic element is present, with hallucinations and delusions to which the patient is reacting, proper sedation—a sedative acting on the midbrain and not on the cortex—produces much more desirable results than a continuous bath or cold packs. Today it is unorthodox to disapprove of hydrotherapy and it may appear reactionary to revert to the use of drugs, but the fact remains that sedation is less of a threat to the ego and arouses less psychic resistance than an enforced “wet cage.” When a patient suffers from insomnia, about which he entertains not only an acute anxiety but also morbid fears as to the grim consequences of his insomnia, it will be much easier to treat him if he succeeds in getting some sleep. His general state will be as improved as that of a so-called normal person who is worn out by lack of sleep. His lessened anxiety will also make him more amenable to deeper treatment. The point may be raised that in the acute confusion states the patient may desire his wet packs or continuous bath as an expression of his unconscious wish, but we still feel that in many situations if drugs can achieve the renewed repression of his unconscious wishes, it may be one step toward our goal. This is by no means an attack on hydrotherapy, which certainly has its place in the treatment of the acute psychoses. It is simply our idea that preconceived prejudices have no place in treatment and that both medication and hydrotherapy have their place.

In intramural treatment psychiatry is faced with certain factors, inherent in the setting itself, which in themselves play a rôle in the patients' recovery. At best the psychiatrist can only adapt his administration and technique so that a positive therapeutic use is made of these conditions. We refer here to group interaction. In exchanging his home setting for the hospital, the patient has laid himself open to new influences which are bound to affect him profoundly. This new group relationship into which the patient enters stimulates new reactions on his part. Since the essence of the therapy must consist of an understanding that the whole difficulty produces a regression in the psyche to an infantile state, the objective of treatment is to lead the patient from the infantile state to as high a level of adult functioning as his capabilities permit. With this in view, the hospital strives to create another home for the patient, but a home in which the stresses, strife, and irritation of his former environment are absent. The hospital, therefore, strives to obviate any but the essential routine that would have to prevail even in a well-ordered home. While rigid schedules, published in a bulletin, look impressive on paper, they make the patient feel like a helpless tool in the hands of another, and this type of routine militates against the psychiatric objectives by destroying the individual's initiative and self-respect and by hindering the develop-

ment of his confidence. In a small set-up like ours it has been possible to create an informal setting, where patients in many ways enjoy both privileges and responsibilities, where rules and regulations are administered discriminately, and where the patient is made to feel that he plays a definite rôle in the running of the place. It is conceivable that in such a setting the head physician represents the understanding father; that the nurse represents the sympathetic mother; and that a relationship with the other patients is established on a sibling basis. With group psychotherapy, permitting free discussion of the individual's problems in the presence of the other patients, a substitute home is organized and the normal sibling relationship is strengthened. By this method other members of the group are encouraged to express their own ideas and even their repressed thoughts which they have not dared to bring to light before.

The rôle that this intra-hospital relationship plays in the lives of patients may be deduced from the fact that an organization begun by expatients only three years ago already has a membership of over three hundred. Their aim is to achieve a permanent society through which they can meet socially and devise ways of being useful to the cause of mental hygiene and particularly to all who are patients at the hospital.

The therapist's rôle in this "family set-up" is consciously to direct the sick person back to his particular maximum degree of adulthood, carefully utilizing the father-and-child relationship, so that the father assumes a diminishing importance as the patient achieves recovery. One must permit the patient to carry out his aggression when it seems advisable and must inflict punishment on him if the aggression is excessive. The attitude of the therapist must be bivalent. He must learn to give affection to the patient and to deny attention when this course is wise. In other words, if the patient continues to demand affection and the more he is given, the more extravagant become his demands, it is necessary to curtail him. It is only when a patient is in a hospital, under constant supervision, that these reactions can be noted. His behavior with the therapist alone and within the group tend to clarify his difficulties and he can be treated accordingly.

Throughout intramural treatment a psychoanalytic understanding of the patient is essential to effective treatment. The intensiveness of the therapy and the degree to which the patient will be permitted and aided to gain insight into his behavior may be guided by other factors. It is our aim to evaluate the patient not only from the material disclosed by himself but also from the information from various other sources, which enables us to gain a perspective of greater totality about the person as a whole. While inevitably there will be a great deal of projection and introjection in this material, it can be examined critically in the light of our observation and knowledge of the patient. It thus becomes possible not only to understand what the patient's problem is, but to prognosticate to some

extent to what type and degree of treatment one can expect receptivity. A psychoanalytic understanding of the patient serves to make every other therapeutic means more effective, whether one has to use hypnosis or whether the patient's intellectual equipment is so minimal that one has to resort to suggestion.

Psychoanalysis is not applicable in a confined environment for three reasons. 1) In the introduction we stated that where a patient becomes socially and economically dependent, it becomes vital to remove him from his home setting. Under favorable economic circumstances it is possible to place such a patient elsewhere under the supervision of a psychiatric nurse and have him brought to the analyst daily. Under such circumstances it becomes possible for the patient to resume his responsibilities when he is ready and to continue with the analysis. In a less favorable economic situation, when the patient resorts to hospitalization, the analytic procedure is generally too expensive and it is unlikely that his family can have him remain under hospitalization for the entire duration of his analysis. Furthermore, it is extremely doubtful whether such a prolonged escape from reality is desirable. 2) The constant exchange of ideas and experiences which is inevitable in a hospital setting is not conducive to positive transference, since there is jealousy and competition unless each patient has a different analyst. 3) Psychiatrists residing in the hospital have to enforce certain rules and the entire approach may become active instead of passive. They have to grant and refuse requests, which interferes with an orthodox analysis.

The most potent medium of treatment in a hospital is intensive, individual psychotherapy which is received by the patient at frequent intervals, each session being of adequate time duration. If the patient possesses good intellectual equipment, adequate background and the type of emotional difficulty that can respond to this treatment, the individual interviews, used in conjunction with group psychotherapy, and the utilization of the other factors in the hospital set-up that may be expected to exert a positive influence, lead to fine therapeutic results. In dealing with those patients who cannot take full advantage of this mode of treatment, the psychiatrist must be prepared to vary his technique to meet the needs of the individual.

Fortunately we have reached a point where the existence of special facilities for borderline patients has ceased to be a controversial subject. On the other hand, differences of viewpoint as to the conduct of such institutions and as to the therapy to be employed are not only desirable but essential, if we are to make progress.

The real issue before us, now that the efficacy of special institutions for voluntary patients has been demonstrated, is to make such facilities widespread and available for all those who require this type of hospitalization. With this in view, it should become the objective of the mental

hygiene movement to foster the construction of small hospitals throughout the state, where early mental patients and psychoneurotics could be treated on a voluntary basis, distinctly apart from the present state hospitals. The creation of such special facilities would encourage patients to accept hospitalization in the early stages of their illness when they are more amenable to therapy, and would eliminate the unnecessary trauma of having such patients classed and housed with incurable cases. Although the additional expense of building and maintaining such units will undoubtedly arouse the opposition of the "tax-minded," their arguments can be met to some extent by the fact that the early institution of treatment will also save the state money by preventing these patients from becoming chronic, custodial cases. The more important issue, of course, is that such a system would save human lives from the waste heap.

DIABETIC ANTERIOR NEURONOPATHY—CLINICAL AND PATHOLOGICAL OBSERVATIONS

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In attempting to reclassify certain nervous diseases on the basis of the neuron, Mills (1) introduced the term neuronitis, making particular reference to multiple neuritis. To him this word seemed to have an unnatural sound and no emphasis was placed on its further employment. Buzzard (2), in discussing the unsatisfactory title of "Acute Toxic Polyneuritis" said that the term motor neuronitis was open to misinterpretation. Subsequently, this designation did not appear in the literature until Kennedy (3) reported four cases of infective neuronitis. These cases were selected from a series published by Bashford, Bradford, and Wilson (4), entitled "Acute Infective Polyneuritis." These authors stressed the fact that their cases represented a definite clinical and pathological entity. Histological studies of seven of these revealed a degeneration of the cells in the ventral and dorsal horns and posterior ganglia of the spinal cord. Similar, but milder, changes were observed in the cells in the deeper layers of the cerebral cortex and pontine nuclei. There also was a patchy neuritis in the peripheral nerves. Kraus (5), in discussing the implication of the peripheral neurons in diabetes mellitus, stated that the clinical evidence indicates involvement of the motor cells and roots, or of the medullary portions of the sensory roots and continuance within the spinal cord. A short time later, Hyslop and Kraus (6) concluded that the motor paralysis of lead intoxication was primarily due to involvement of the anterior horn cells and insisted that this process should be regarded as neuronitis.

Recently, Griggs and Olsen (7), in discussing the changes seen in the spinal cord in diabetes mellitus, stated that three types of lesions may occur. These are: degeneration of the motor cells of the brain stem and spinal cord; degeneration of the intramedullary portion of the dorsal root fibers with secondary system degeneration; and funicular necrosis of the posterior columns. Clinically, these present three varieties of syndromes; namely, that of the so-called chronic anterior poliomyelitis with little or no sensory changes; the syndrome of degeneration of the dorso-lateral tracts; and, finally, the picture of tabes dorsalis. These authors describe a case with autopsy findings showing degeneration of the dorso-lateral tracts of the spinal cord.

The following two cases of diabetes mellitus with neural involvement demonstrate the changes in the anterior horn cells.

CASE REPORTS

Case 1. History (Adm. 391478). A. B., a widow, aged 65 years, was admitted to The Mount Sinai Hospital on March 31, 1936. Hypertension had been present for many years and glycosuria for the past three years. During the previous year she had received thirty-five units of insulin daily. For the past five months, the patient had complained of gradual weakness of the right lower extremity and severe pain in the right thigh. These had become so intense that she had been confined to her bed for the six weeks prior to admission. During that time, weakness of the left leg had appeared. A few weeks later, the patient awoke with pain along the eighth and ninth ribs on the lateral aspect of the left side of the chest. This pain had been intermittent and the area was constantly tender. At the time of admission she complained of pain in the right lower extremity.

Examination. The patient was emaciated and completely blind. Examination of the cardiovascular system disclosed that the heart was enlarged to the left; A_2 was greater than P_2 ; and there was sclerosis of the peripheral arteries. The blood pressure was 150 systolic and 94 diastolic. The veins of both legs were solidly thrombosed and felt like cords. External and internal hemorrhoids were present. There was tenderness over the sixth and seventh ribs in the right axillary line.

Upon neurological examination, the right pupil was found to be larger than the left. The retinal vessels were sclerosed and small hemorrhages were seen in the left retina. There was a flaccid paralysis of the right lower extremity with marked weakness and flaccidity of the left lower extremity. Muscle atrophy was marked in both lower extremities, especially on the right. The deep reflexes were completely lost in the lower limbs and diminished in the upper limbs. The abdominal reflexes were absent.

Laboratory Data. The urine contained 5 per cent sugar. The blood sugar estimation was 300 milligrams per cent. The cerebrospinal fluid contained six cells per cubic millimeter, all of which were monocytes. The Pandy reaction was positive. Roentgenological examination disclosed a generalized osteoporosis of the ribs, scoliosis and a moderate degree of hypertrophic spondylitis of the spine. The blood vessels of the lower extremities were seen to be markedly calcified.

Course. The diabetes was adequately controlled and the pain in the right leg became less severe after a short while. The diagnostic possibilities considered were: myelopathy on an arteriosclerotic basis, malignancy and diabetic anterior neuronopathy. The latter diagnosis was suggested by Dr. Globus because of the exclusive involvement of the lower motor neuron.

On the fifth day after admission, there was profuse rectal bleeding which continued for almost two days. This was severe enough to produce shock. A transfusion of 500 c.c. of citrated blood was given and on the following day the bleeding stopped and the patient's general condition improved. After a short while, there appeared an aphthous stomatitis with lesions on the soft palate and inner surface of the lower lip. Shortly following this, a sacral decubitus abscess was incised and drained. This healed slowly. Subsequently, her general condition improved so that she no longer complained of pain. However, on May 30, 1936, a tender area of fulness with superficial crepitation in the left costo-vertebral angle appeared. This was incised and irrigated. A culture from the wound was reported as *Enterococcus*. Two days later the patient lapsed into a stuporous state from which she could not be aroused. A febrile reaction followed and she died on June 2, 1936 with a terminal temperature of 104.4°F.

Necropsy Findings. Only the lower cord with the attached roots of the cauda equina was removed. It was shrunken and felt rubbery. In cross section it appeared as if there were several areas of softening, but later examination proved that these defects were due to the effects of trauma consequent to removal.

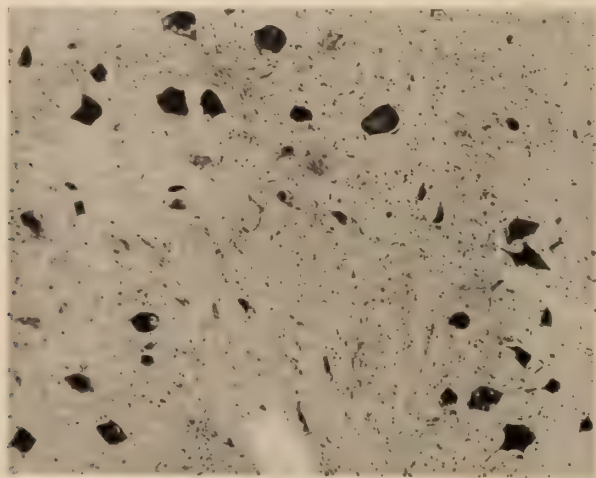


FIG. 1. Photomicrograph showing degenerated anterior horn cells in the spinal cord. Note the vacuolization (Nissl stain).

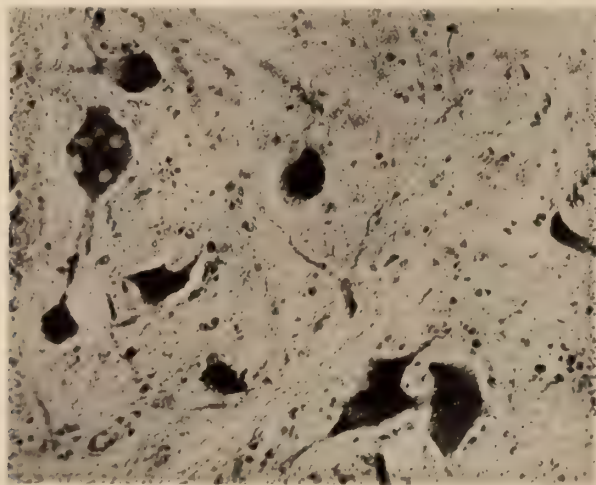


FIG. 2. Higher power photomicrograph showing degenerated anterior horn cells

Methods. The material was fixed in formaldehyde. Paraffin, celloidin and frozen sections were prepared. The stains employed were hematoxylin and eosin, Nissl, Spielmeier, Pal-Weigert, and Weil for myelin sheaths; Scharlach R, Nile Blue, and Marchi's osmic acid stain for fat; Holzer, Bielschowsky, the Globus modifications of the Cajal gold chloride and Hortega silver impregnation methods.

Microscopic Anatomy. Hematoxylin-eosin and Nissl stains revealed that there was marked degeneration of the ganglion cells of the anterior horns. One side was more extensively involved than the other. Some cells were large, swollen, and pear-shaped, while others were small and shrunken. Numerous cells were devoid of nuclei. The cytoplasm was granular, darkly staining and vacuolated. The nuclei

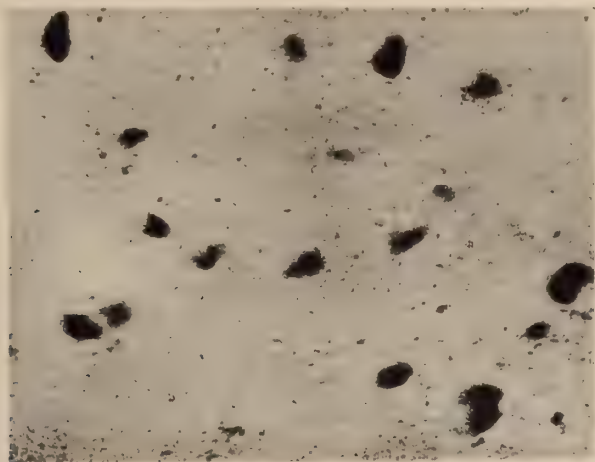


FIG. 3. Photomicrograph showing dense accumulation of fat in anterior horn cells of spinal cord (Scharlach R. stain).

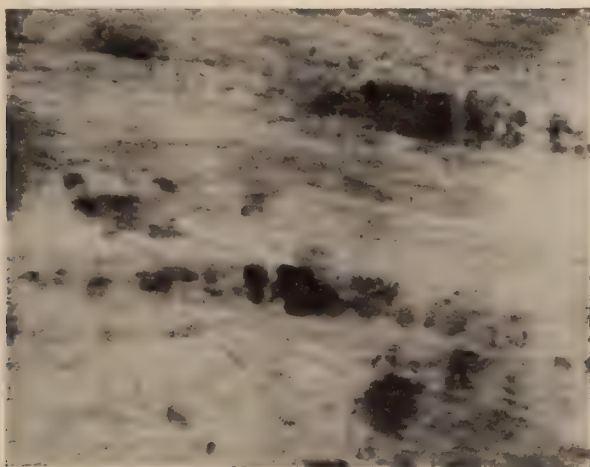


FIG. 4. Photomicrograph of longitudinal section of peripheral nerve, demonstrating the presence of fat (Marchi stain).

were small and shrunken, but otherwise large and eccentric (Figs. 1 and 2). Fat stains disclosed that a number of cells was completely replaced by fat, while the majority contained more than the normal amount of lipoid substance (Fig. 3). This was present at all levels. Glia elements were prominent around the anterior horn cells, especially those which showed degenerative changes.

However, by the Marchi osmic acid method, it was possible to demonstrate the presence of diffuse myelin degeneration in the spinal cord. The nerve roots of the cauda equina displayed marked degenerative changes (Fig. 4). The anterior nerve roots showed similar changes, but to a lesser degree.

The blood vessels revealed a moderate amount of arteriosclerosis. Some fatty degeneration was seen within their walls. This was most evident in the small vessels within the gray matter of the cord. The ependymal lining of the central canal was disorganized with proliferation of the ependymal cells. The meninges displayed a slight amount of fibrous thickening. Amyloid bodies were present.

The pathology in this case involves almost selectively the anterior horn cells and for this reason the term neuronopathy seems especially appropriate. The other changes observed may be considered secondary to the damage to the neuron. The specificity of this disease process is reflected in the clinical findings of areflexia, flaccid paralysis, and muscular atrophy. Further, a greater number of anterior horn cells were more involved on one side than on the other, and, clinically, the right lower extremity displayed more impairment than the left.

The vascular alterations are of interest. Although a peripheral arteriosclerosis was noted, the arteriosclerotic process in the blood vessels of the spinal cord was not marked. The moderate degree of vascular changes present were in the small intramedullary blood vessels. From the Marchi osmic acid preparation it could be seen that this damage was of relatively recent occurrence and could logically be considered as part of the same process that effected the neuronopathy. Similarly, Hyslop and Kraus (6), in their critical review of the pathology of lead intoxication, concluded that the toxic agent responsible for the paralysis selectively damaged the blood vessels and gray matter of the spinal cord.

Case 2. History (Adm. 406705). A. O., a tailor, aged 68 years, was admitted to The Mount Sinai Hospital on April 4, 1937. At the age of twenty-eight the patient suffered an acute illness characterized by high fever, severe headaches, and marked prostration for several weeks. At this time there was observed an area of analgesia over the lateral surface of the left thigh. For the past fifteen years he had had diabetes mellitus which was controlled by dietary means until three years previously. Since that time he had been receiving twenty units of insulin daily because of continued glycosuria. During the previous five years, he had had two attacks of left loin pain relieved by cystoscopic manipulation. Four months before, the patient began to experience painful sensations along the lateral surface of the left thigh. During the past two months severe shooting pains radiating from the external surface of the left thigh down to the ankle were present. In addition, he had noticed weakness and paresthesias in this limb.

Examination. The peripheral blood vessels were moderately sclerotic but their pulsations were nevertheless evident. The blood pressure was 166 systolic and 86 diastolic. The heart sounds were of good quality. There were cataractous changes in the lenses of the eyes. Upon neurologic examination, atrophy and tenderness of the musculature of the left lower extremity, together with fibrillations of the thigh muscles, were noted. The tendon reflexes were depressed on this side. There was diminution of cutaneous sensation in the distribution of the left lateral femoral

cutaneous nerve. The diagnosis at this time was neuronopathy affecting the anterior horn cells and roots of the lumbosacral region, most likely on a diabetic basis.

Laboratory Data. Lumbar puncture revealed an initial pressure of 60 cubic millimeters with no evidence of a block in the subarachnoid space. The blood sugar estimation was 170 milligrams per cent. The quantitative urinary sugar determination was 1.8 per cent. Roentgenological examination failed to show any abnormality in the bones of the pelvis and left lower extremity. The electrocardiographic tracings disclosed "probable involvement of the ventricular muscle."

Course. The diabetes was well controlled on thirty units of insulin daily. After a few weeks the pain had subsided and the muscle tenderness became less marked. However, the depressed tendon jerks, fibrillations, and cutaneous changes remained unaltered.

With the exception of the findings of an old meralgia paresthetica, the objective signs indicated involvement of the anterior horn cells and anterior roots of the lumbosacral region of the spinal cord. As far as could be demonstrated clinically, the remainder of the spinal cord was unaffected by the pathologic process.

COMMENT

In the light of present knowledge no definite statement can be made as to the pathogenesis of spinal cord damage in diabetes mellitus. Bumke and Foerster (8) quote Kostakoff, who stated that the ketone bodies slowly produce changes in the anterior horn cells. In several of the cases reported by Jordan (9), this author has found that with the correction of the hyperglycemia and maintenance of the blood sugar at a normal level there followed a disappearance of the neural symptoms. Vitamin insufficiency has long been recognized as a probable factor. However, even with the addition of vitamins, improvement does not always take place. It is possible that, in some of these cases, the difficulty is in absorption or utilization rather than in consumption. Arteriosclerosis may be responsible for the changes observed, and is present in a great number of cases. Certainly it is not the chief cause, since it is well known that even when the arteriosclerosis is so advanced that the lower portions of the legs are dusky-red, there is no indication of neuronopathy. Griggs and Olsen introduce the possibility that the alterations in the spinal cord may be due to reduction in the blood supply because of sclerosis of the vessels effecting a diminished tissue resistance, and thus favoring the action of other etiologic agents.

This work has been done under the supervision of Dr. Joseph H. Globus for whose kind guidance I wish to express my thanks.

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PSYCHOTIC MANIFESTATIONS IN DISSEMINATED SCLEROSIS

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The experience of most neurologists is that pronounced psychotic manifestations in disseminated sclerosis are rare. The psychic symptoms in this disease have received comparatively little attention, as they are very often overshadowed by the organic nervous symptoms. Scanning the rather extensive contributions on the subject, it becomes apparent that there is a great variety of opinion. The individual symptoms are reported either as rare, or as present in all cases.

Incidence. In the average general hospital, the routine often militates against complete psychiatric examinations on ward patients. Patients with mental disturbances, not being amenable, as a rule, to the hospital discipline are soon discharged or transferred to a state hospital. And so it is from the state hospitals that we may learn of the incidence of psychosis with multiple sclerosis. Among 29,700 first admissions to the Massachusetts State Hospitals from 1918 to 1925, inclusive, there were only twenty cases. An even smaller proportion is reported by Brown and Davis (1), who found only three cases among 6,700 admissions to the Manhattan State Hospital. The explanation for the discrepancy in the figures is either that many cases are not committed because they are physically incapable of performing acts which might lead to commitment or that it is uncommon for the mental symptoms to be sufficiently severe to necessitate treatment in an institution for mental illness.

Types of Mental Symptoms. The observations of Brown and Davis indicate that the mental symptoms in this disease are so diverse, that a consistent group of symptoms can not be formulated. They divide the mental symptoms into two groups; first, those which are primarily and directly the result of the organic lesions, such as euphoria, confused states, hallucinations, mental defect and Korsakoff's syndrome, as well as the occasional terminal states with delusions of grandeur; and second, those which are functional. In this group they place those transitory delusional states and depressions which appear to arise as a result of the incapacity in which the patient finds himself. Jelliffe (2) stresses inherent emotional and psychological factors in the development of psychic alterations in multiple sclerosis.

Barbu (3) states that there are three groups of psychic disturbances which occur in disseminated sclerosis: (a) euphoric dementia with peculiar childish behavior, heightened suggestibility and disturbances of memory;

(b) states resembling other psychoses, but of milder form; and (c) hysterical manifestations. Cohen and Gavigan (4) believe that the psychiatric manifestations, for practical clinical purposes, can be grouped into four categories: (a) as personality changes; (b) as expressions of the patient's experience of the disease; (c) as psychotic symptoms, perhaps directly referable to the location of the plaques; and (d) as a known, generally recognizable, though etiologically uncertain, disease entity such as schizophrenia or manic depressive psychosis.

EMOTIONAL DISTURBANCES

Euphoria. By far the most constant emotional state is one of euphoria or mild elation, varying degrees of which have been noted by all observers. It is present in the great majority of cases, and in its simplest form, is manifested by a far more hopeful attitude on the part of the patient than his physical state would seem to warrant. The common feeling of emotional or affective well-being is sometimes designated as euphoria sclerotica, and the undue optimism is called spes sclerotica. Brown and Davis point out that the euphoria is simply an "inconsistency of mood and physical disability," but it is so constant a finding, that it must be considered a general characteristic of the disease, rather than a matter of the individual's make-up. There has also been described a feeling of physical well-being called eutonia. This is said to be less frequent than the euphoria.

Uncontrollable Laughter and Crying. Outbursts of laughing and crying of an uncontrollable character, not necessarily accompanied by an appropriate change of mood, are not infrequent. Regardless of the patient's condition and environment, he cannot refrain from laughing in a loud and distressing manner. There is some question as to whether these attacks may be ascribed to emotional instability or have an anatomical origin in the involvement of the thalamus or the cortico-bulbo-cerebellar pathways.

MENTAL ENFEEBLEMENT

This group of mental symptoms includes intellectual, attentive, memory and emotional disorders, occurring in various combinations, and evidenced by slowness of thought, lack of power of concentration, failure of memory, apathy and indifference. In comparison with the affective symptoms, intellectual disorders are minimal and negligible. Coupled with the euphoria, and probably dependent upon it, there is a lack of insight for the seriousness of the illness. As would be expected in an organic condition, the memory is affected in a certain proportion of cases. That it is not more frequently affected depends presumably upon the limitation of the sclerotic processes to lower levels of the nervous system.

DIFFERENTIAL DIAGNOSIS

Hysteria. Early in its course disseminated sclerosis, especially if it is accompanied by emotional changes and impulsive laughter or crying,

may be mistaken for hysteria. It is not surprising that such a mistake should be made, considering the age of incidence, the type and fleeting nature of the neurological symptoms, and the occurrence of uncontrollable laughter and crying in disseminated sclerosis, especially in those cases in which the Charcot triad of nystagmus, scanning speech and intention tremor, is not a prominent feature. However, organic signs such as absent abdominal reflexes, a Babinski sign, optic atrophy, etc., do not occur in hysteria. The characteristic mental attitude in the latter condition is the "belle indifference," which contrasts to some extent with the positive euphoria of disseminated sclerosis. The two diseases may, however, coexist. In fact, it has long been recognized that hysteria is a very frequent and conspicuous complication of disseminated sclerosis.

General Paresis. When euphoria develops early, as is frequently the case, or when the disease is accompanied by marked grandiose delusions, or a gradually progressive mental deterioration, or, on the other hand, when the distribution of the sclerotic patches is quite similar to the distribution of the lesions in general paresis, the symptoms may lead to confusion in diagnosis. There is not a single neurologic sign or psychologic symptom of general paresis which may not be seen in disseminated sclerosis. The tremor may not be coarse and widely ataxic, but may resemble that of paresis; this resemblance is also noted in the speech disturbances. At the same time, a typical expansive mental state may make its appearance. After a while, the mental symptoms may recede and a mild dementia with some depression may remain. As the disease progresses, the signs of disseminated sclerosis become more apparent and the diagnosis becomes clear. Diagnostic problems, however, can be cleared up by the laboratory findings. It must be borne in mind that many cases were observed prior to the days of the Wassermann test and the discovery of the spirocheta pallida. Without modern methods, there would be danger of confusion of the two diseases even on histological examination or serological findings (paretic colloidal gold curves of the spinal fluid are not infrequent in disseminated sclerosis) with the exception, of course, of the positive Wassermann reaction in general paresis. The probability is that most of the mixed cases formerly described were cases of pure disseminated sclerosis. The clinical picture is neither that of classical paresis, nor that of cerebral arteriosclerosis, but may be more like that occasionally seen in brain tumor.

Schizophrenia. Less frequently does disseminated sclerosis with mental symptoms simulate schizophrenia. With the euphoria, there may be some dissociation of affect, or a disharmony between the emotional reaction and the thought content. However, marked distortion of thought and oddities of conduct, which are so frequent in schizophrenics, are not encountered in disseminated sclerosis. Occasionally a patient may be suspicious and paranoid. Others are silly, smiling and giggling without sufficient

provocation or apparent cause. Persecutory and grandiose delusions, sometimes of a bizarre type, as well as auditory and visual hallucinations, may occur. There is no correlation between the parts of the body showing the most intensive effects of the disease and the content of the delusional or hallucinatory trends. Hallucinations and ideas of reference may represent unadjusted aspects of the personality which have been projected because of the disturbance at the organic level. It is reasonable to suppose that the secondary symptoms, such as depressed and paranoid states, depend to a considerable extent upon the mental make-up of the patient before the disease developed. With the primary mental symptoms of the disease this is not the case, and although the latter are quite variable, they are not more so than are the physical symptoms.

CASE REPORTS

Disseminated sclerosis manifesting schizophrenic symptoms of the paranoid type

History. G. P., a thirty-six year old Hebrew male, a trainman by occupation, was admitted to the Morrisania City Hospital on March 10, 1937, complaining of staggering, weakness of his legs, electric shocks running through his trunk and extremities with each step, and an "abnormal" feeling of both hands. At first, he was uncooperative, seclusive, and suspicious, refusing to give his right name or race, but finally when he became more confident of the trustworthiness of his interrogator, he acknowledged them and revealed that there was no nervous or mental disease in the family. However, for an indefinite period he had had considerable domestic difficulties, the nature of which he would not disclose. In the winter of 1928, he slipped and fell on an icy pavement, but did not strike his head. He recalled that he was unable to move until he was helped to his feet. About a year later, he stepped into a hole and felt a sensation like an electric shock running through his body and out into his arms and legs. Following that, and until quite recently, this sensation was reproduced with each step. He was seen at the Hospital for Joint Diseases, where an X-ray examination of his spine revealed only some slight arthritic changes. In 1935, in the course of an altercation, he received two blows on the right side of his jaw. From this incident, following which he was dazed for a number of hours but did not lose consciousness, he dates the onset of his staggering. This was not lateralized and has been progressive. For the last few months, he stated that he had been dragging his left leg and this, too, had become progressively worse. The dysesthesia of his hands began about 1925, when they may have been frost-bitten.

Examination. The patient's speech was monotonous, slurred, somewhat ataxic and occasionally propulsive. His facies was slightly fixed and the skin was red and oily. The pupils were equal, regular and reacted to light and in accommodation. The fundi oculi showed a well marked bitemporal pallor of the optic discs. Nystagmus was present in both lateral planes. There was some weakness of convergence in the right eye. The left eyeball did not turn in nasally as well in right conjugate gaze as in convergence. The right palpebral fissure was greater than the left. The left nasolabial fold was flatter than the right. There was slight bilateral impairment of hearing of the perceptive type. Slight tremor of the tongue and slight intention tremor of both hands were present. The tendon reflexes in the upper extremities were diminished, but were hyperactive in the lower extremities. The right supra-patellar reflex was greater than the left, but the left knee jerk was more active than

the right. A bilateral Babinski sign was present. The abdominal reflexes were not elicited. Errors in position sense in the small toes of the left foot and slight impairment of pallesthesia over the left internal and external malleoli were noted. Slight ataxia on finger-to-nose and heel-to-knee tests was also noted. The gait was ataxic, with some dragging of the left leg, apparently due to spasticity. The general medical examination was essentially negative.

Mental Status. The patient was neat and tidy in his general appearance. He was cooperative and garrulous. His verbal responses were fragmentary, at times incoherent and irrelevant, and showed definite flight of ideas with perseveration of speech and circumstantiality. He was euphoric but also irritable at times. Orientation in all spheres was correct. He said; "nine times nine is eighteen." Memory was defective for both recent and remote events, and there was also some defect in attention and comprehension. He was somewhat delusional, suspicious, seclusive with mild persecutory ideas and ideas of reference. He showed some emotional deterioration, dissociation of affect, poor insight and judgment. He denied any disability and there was complete repression of the idea that he was ill.

Laboratory Data. Blood pressure was 110 systolic and 90 diastolic. The hemoglobin was 103 per cent; color index .98; red blood cells 5,280,000; white blood cells 6,850, polymorphonuclear neutrophils, 78 per cent, lymphocytes 18 per cent and mononuclears 4 per cent. The urea nitrogen was 18; creatinin 1; sugar, 86 mg. per 100 c. c. of blood. The blood Wassermann test was negative. The cerebrospinal fluid was under normal pressure and contained 4 cells; the globulin was negative; the total protein, 41 mg., the Wassermann test was negative; the colloidal gold curve was 1111100000. A roentgenogram of the skull was reported as showing mild arteriosclerosis. An X-ray examination of the spine was reported as apparently normal.

Manic and Depressed States. In a small proportion of patients, there is a mild depression. Fleeting attacks of depression occur rather frequently, and may be merely an evidence of the general emotional instability; perhaps, too, as a reaction on the part of the individual, to the sudden realization that he cannot, as he formerly did, pursue his regular activity or gainful occupation, that he cannot compete with others in physical endeavors. Prolonged depressive periods with suicidal ideas are relatively rare. In most cases the mood varies readily, but a few are dull and apathetic, and some are irritable. Others show a true autonomous depression, and some are pathologically euphoric or manic.

RELATION OF PSYCHIC DISTURBANCES TO ANATOMIC BRAIN CHANGES

The relation of the psychic disturbance to the anatomic changes found in the brain is still controversial. Cases have been reported with euphoria, indifference and dullness, and mental depression with pronounced suicidal tendency, in which histological examination of the cerebral cortex failed to disclose any foci of disease. On the other hand, cases in which the brain has shown the most marked involvement have been noted to develop mental symptoms earliest and to undergo the most rapid and complete mental changes. Taylor (5), in a series of fourteen cases, attempted to correlate the neurological and mental findings during life with the necropsy findings. He concluded that, as in other structural diseases of the nervous system, a general correlation between certain symptoms and lesions in

certain localities could be made, but that a precise determination of lesions from symptoms and symptoms from lesions was not possible on account of the peculiar type of degeneration in the disease, particularly the long persistence of axones, the resistance of the cells and the multiplicity of lesions, all of which confuse the clinical picture. One is not justified in attributing mental changes to lesions of the cortex, when association tracts and deeper structures are also involved.

Many believe that the psychic symptoms are consistent with the mental make-up of the patient and may be activated by the disease. Cohen and Gavigan quite correctly state that "every sick individual experiences his illness in a manner which is in accordance with his personality make-up. A patient, recognizing the fact that his illness is chronic, disabling and incurable, may manifest resignation, resentment, depression, anxiety, cheerfulness—any or several of these expressions."

Cottrell and Wilson (6), associate the invasion of the affective sphere with the pathologic fact that the disease almost constantly shows a periventricular, subependymal spread; and correlate the relative integrity of the intellectual faculties with the relative conservation of the cortex, unless, indeed, the disease is far advanced. Evidence was adduced by them, suggesting that the affective manifestations are the outcome of the invasion by the morbid process of the paleothalamus, and that they may arise before structural disease of the neuraxis is clinically apparent. This they set down to dynamic alteration of function, of toxic origin. They also indicated that certain psychoses and psychoneuroses associated with disseminated sclerosis, and characterized by changes in the affective field, may have a toxic or toxi-structural and not a psychopathological basis.

Howes (7), suggested that since disseminated sclerosis and lues may produce similar lesions and clinical pictures, disseminated sclerosis may actually be the result of an infectious and toxic process, similar to that of neurosyphilis. Further, inasmuch as in the latter disease it is generally felt that there is a definite anatomic basis for the mental symptoms, it is possible that such an explanation may also apply to the mental symptoms of disseminated sclerosis.

Barbu reported two cases of disseminated sclerosis with necropsies, and was uncertain which of the two chief pathologic changes discovered was the cause of the intellectual decline: the cortical damage produced by the meningeal fibrosis, or the sclerotic patches.

It would seem that the meningeal fibrosis with its consequent brain atrophy would be more likely to cause the memory disturbances and that the disseminated foci could be the cause of the mental symptoms. Both of these factors may have their bearing in individual cases, but they do not explain the majority of cases. It would be surprising if the lesions themselves did not occasionally produce symptoms, depending upon their locations. The more uncommon symptoms, for example, the delusional

trends, hallucinations and the large group of atypical symptoms, may possibly be explained on this basis. The personality element may serve to determine the nature of the emotional state. So far, no one has conclusively demonstrated the mechanism by which these mental symptoms are produced in disseminated sclerosis.

Our only suggestion is that, inasmuch as mental illness is fairly common among the general population, it is to be expected that among these there should be cases who later develop disseminated sclerosis. Furthermore, patients with this disease may eventually become conscious of their physical handicap. This, in turn, may bring into play subconscious mental mechanisms in an attempt to adjust the organism to the environment, or to compensate for the feeling of inferiority; failing in this, there may be regression to a level at which the patient is comfortable. It is within the realm of possibility, in some instances, that disseminated sclerosis may precipitate either a schizophrenic or a manic depressive reaction. The slighter mental changes may be partly a reaction to the victim's knowledge of the presence of the disease and partly a result of his physical weakness and discomfort. The individual afflicted with disseminated sclerosis may also have superimposed mental factors derived from the immediate environment and may find it arduous to face painful situations or to adequately repress them. He may surmount one or more difficulties successfully, only to succumb before an accumulation of troubles. We must therefore conclude that it is futile to attempt to correlate the psychotic symptoms with specific anatomic changes in disseminated sclerosis. Many different causes must be present to produce marked psychic disturbances.

SUMMARY

Mental symptoms do not always occur in disseminated sclerosis, although they probably appear in a large proportion of cases. While they are not usually prominent, they may be of wide variety. One of the most frequent manifestations is a certain amount of mental deterioration, shown by impairment of memory, slowness in stream of thought and emotional indifference. When disseminated sclerosis begins in early life, it usually has particularly serious results psychically and may jeopardize further mental development. On the other hand, where hallucinations and delirium have been described, there is certainly a combination with a psychosis. Psychic alterations often occur after a long period of an apparently normal mental condition. Late in the disease, in a fairly large number of cases, we are apt to find mental aberrations.

From the very nature of its pathology it is not surprising to find that, clinically, disseminated sclerosis may simulate any other brain or nervous disease, both from a mental and a physical standpoint. Strangely enough, the mental symptoms may, like the neurologic signs, be inconstant,

shifting and undergoing complete remissions at any time in their course. It is certain that patients with this condition may manifest psychic symptoms which antedated the disease, and that they may also have a superimposed psychoneurosis or a functional psychosis.

It is likely that mental disturbances of varying grades are present in a larger percentage of the cases of disseminated sclerosis than has been reported by neurologists. Routine psychiatric examinations, with more emphasis on the psychobiologic viewpoint, and a keener cognizance of the possibility of concomitant psychologic alteration may uncover more cases.

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CONTRACTIONS IN DENERVATED MUSCLES INDUCED BY FRIGHT AS EVIDENCE OF SECRETION OF A PARASYMPATHETIC HORMONE*

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It is well known that under conditions of severe emotional excitement, such as fear and rage, or during vigorous muscular exercise, the autonomic nervous system is strongly activated. Numerous studies have shown that the autonomic nerve fibers exert their effects through the medium of specific chemical agents. Evidence has accumulated indicating that an adrenaline-like substance is elaborated at the endings of sympathetic or adrenergic nerve fibers (1). There is similar evidence that a substance like acetylcholine is formed at endings of parasympathetic or cholinergic nerve fibers (2). These humoral substances are set free near, or within, the tissues of responsive visceral end organs by nerve impulses, and play an important rôle in the functional control of the organs innervated.

That adrenaline is liberated during emotional stress has long been known, but although there are signs of parasympathetic activity, no one has previously demonstrated the liberation of acetylcholine during fright. To recover acetylcholine from the blood of an excited animal is difficult, especially because this substance is so rapidly destroyed by body enzymes. In this communication, an attempt will be made to bring forth biologic evidence for the secretion of a parasympathetic hormone in the body during fright.

It is an established fact that denervated muscles, when in contact with acetylcholine, go into a slow contraction.¹ The occurrence of a contraction in denervated paralyzed muscle may thus be used as an indicator in the detection of acetylcholine (3).

All observations were made in animals which were allowed to run loose in their cages. Under such conditions, the best visualization of contractions could be obtained in muscles of the face and eye, because a contraction in facial or ocular muscles of one side could easily be detected by the resultant distortion of the face or alteration in size of the palpebral aperture. Therefore, the peripheral motor nerve supply to facial or ocular muscles of monkeys was completely destroyed.

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¹ Several theories have been advanced for this phenomenon, but none has been universally accepted.

Following a period allowed for nerve endings to degenerate (usually six to eighteen days), it was noted that contractions of the paralytic muscles occurred whenever the monkey was angered or frightened. In the cases with facial denervation, the face twisted to one side and the palpebral fissure narrowed, while in the cases with oculomotor denervation the drooped eyelid retracted. For simplification, the contractions in the denervated muscles following fright will be designated by the term "fright reaction." The method commonly employed to frighten the monkey was to threaten it with objects such as sticks, black rubber hose, or a monkey-catching net. While the animal was thus frightened, it ran around the cage dodging the menacing object. About two or three seconds after the threatening had been stopped, contractions of the paralyzed muscles appeared. The contractions were slow and persisted for fifty seconds. When evidence of nerve regeneration appeared, the fright reaction began



FIG. 1. *A.* Facial expression at rest.

B. Lack of blink response in left eye, due to facial paralysis.

C. Contraction of denervated muscles of left side of the face, induced by fright. Note the marked twisting of the face, lips and nostrils to the left, sphincter-like narrowing of the palpebral fissure, and increased wrinkling of the face on that side. The same type of contraction in the denervated muscles occurred immediately after the monkey recovered from an anesthetic, or whenever it was exposed to a cold atmosphere.

to diminish. As long as the muscles remained denervated, they contracted in association with fright. These phenomena seemed to suggest the possibility that the contractions were due to the secretion of a substance to which the denervated muscles were sensitive—that is, acetylcholine. Acetylcholine has been found to be a natural constituent of the body (4).

The fright reaction was obtained in every animal tested and was invariably augmented by a previous intramuscular injection of eserine. Since it is well known that eserine acts by potentiating acetylcholine through the inhibition of choline esterase (5), the enzyme which destroys acetylcholine, the intensification of the contraction by eserine seemed to be further proof that the fright reaction was effected through a substance similar to acetylcholine. Contractions in these denervated muscles could be reproduced by intramuscular or intravenous injections of acetylcholine. In order for intramuscular injections of acetylcholine to be effective, it was

necessary to eserinize the animal. Intravenous injections of acetylcholine were effective even without eserization, and in either case the visible contractions lasted thirty to forty seconds. The contractions induced by intramuscular injection lasted anywhere from one to thirty minutes; the usual duration, however, was between five and ten minutes.² All intramuscular injections were made in the shoulder or thigh muscle groups and not in the denervated muscles. The contractions induced by drugs were strictly parallel to those associated with fright. In each instance, the phenomenon occurred only after a period allowed for nerve endings to degenerate, and it disappeared when nerve regeneration became manifest.

Other drugs injected were atropine and adrenaline. Atropine, which has been found to counteract the muscarine effects of acetylcholine, did

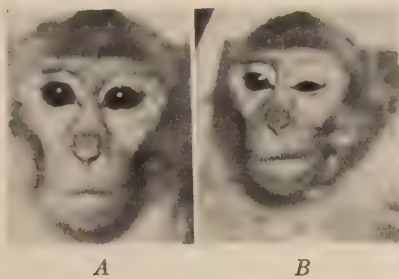


FIG. 2. The left facial nerve of a blind and hemiplegic monkey was resected at its exit from the stylomastoid foramen, on March 22, 1937. Contraction in the denervated muscles induced by fright and those reproduced by drugs first appeared on March 29, 1937.

A. Facial expression at rest.

B. Contractions in denervated muscles reproduced by the injection of eserine and, fifteen minutes later, of acetylcholine into the deltoid muscle. Adrenaline injected at this stage slightly inhibited the contractions; i.e., the fissure became less narrow and the mouth was not as twisted to one side.

not have any visible influence on the state of contractions of denervated muscles following fright, or those reproduced by acetylcholine (6). Adrenaline, which is known to be secreted during fright, never caused contractions in the denervated muscles. Indeed, not only did adrenaline fail to yield contractions, but it actually inhibited the contractions induced by fright or with acetylcholine (6).

From the foregoing data, it appeared that there was almost a strict parallelism in the behavior of the contractions under conditions of fright and those reproduced by the parasympathicomimetic drug, acetylcholine.

² These observations suggested that (a) acetylcholine may persist in the body tissues for long periods. (Only when acetylcholine enters the blood stream is it rapidly destroyed.) (b) Eserine enhances but does not prolong the action of acetylcholine through the blood stream.

Since it is well known (a) that denervated muscles are sensitive to acetylcholine, (b) that the action of acetylcholine is augmented by eserine, (c) that atropine does not completely neutralize the nicotine effects of acetylcholine, and (d) that adrenaline slightly inhibits the action of acetylcholine,

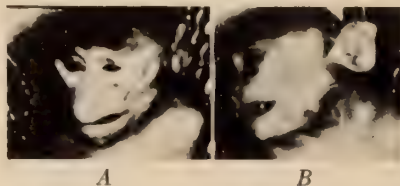


FIG. 3. *A*. Contractions in denervated muscles induced by fright, even after the homolateral infraorbital nerves and the superior cervical ganglion were resected.

B. A severe contraction causing the upper lip to be raised and exposing the teeth. In this animal, the sensitization effect by acetylcholine and by adrenaline could be obtained at the same time. Intramuscular injection of eserine and acetylcholine produced a marked spasm in the left side of the face. At this stage, intravenous injection of adrenaline produced a marked blanching of the left side of the face, blushing of the right side of the face, and dilatation of the left pupil. The contractions in denervated muscles were slightly lessened by adrenaline.



FIG. 4. Various stages in the opening of the drooped eyelid, effected by intra-muscular injection of eserine-acetylcholine. The photographs were taken several seconds apart. The same degree of opening could be induced by frightening the animal.

it seemed safe to assume that the contractions in denervated muscles obtained with fright, which exhibited the above properties, were due to a substance similar to acetylcholine, which came in contact with these muscles. Especially may this be true because the fright reaction occurred as long as the muscles remained denervated.

Assuming that the contractions were due to a substance secreted during fright, experiments were carried out to determine whether this substance, acetylcholine, reached the muscles in question through the local vasodilator nerve supply or by diffusion from the general circulation through the capillary walls in contact with these muscles. Dale and Gaddum (7), among others, suggested that stimulation of the vasodilator nerve fibers of arterioles caused a liberation of acetylcholine at the nerve endings and in turn the liberated substance became diffused to the local denervated muscle fibers; the fibers, owing to their sensitization to acetylcholine, contracted. The autonomic nerve supply to the blood vessels of the ocular muscles is derived mainly from the cervical sympathetic, while nerves of blood vessels to the face originate from the cervical sympathetic and infraorbital nerves. With this in mind, the following experiments were carried out to determine whether the contractions in denervated muscles were due to a local effect.

Stimulation of the cervical sympathetic trunk produced the usual dilatation of the pupil, slight exophthalmos, and piloerection of the face. No contractions were visible in the homolateral denervated muscles, even after strong faradic current was applied. In animals with ophthalmoplegia, stimulation of the cervical sympathetic caused a slight elevation of the drooped eyelid, but the degree of elevation was not more than that observed in the normal eye. The slight opening of the lids thus obtained never compared with the marked retraction of the ptosed lid associated with fright.

These negative findings are stressed because Rogowicz (8), in 1885, working with denervated facial muscles of a dog, found that by stimulating the cervical sympathetic, contractions in muscles of the upper lip occurred. The contractions were feeble and were localized chiefly to the zygomaticus.

Section of the cervical sympathetic trunk or extirpation of the superior cervical ganglion on the side of the denervated muscles, or even bilaterally, did not prevent the occurrence of the fright reaction.³ Stimulation of the infraorbital nerves, which form an intricate plexus with branches of the facial nerve, yielded no responses in the homolateral denervated muscles (10). Again, resection of the infraorbital nerves, with or without resection of the cervical sympathetic, did not in any way lessen the degree of contraction associated with fright. Resections of both facial or of the homolateral oculomotor or trochlear nerves, were also without effect on the state of contraction in denervated muscles. In other words, neither stimulation nor resection of these nerves had any visible effect on the state of the paralyzed muscles.

These experiments seemed to demonstrate that the fright reaction was not due to secretion of acetylcholine from local nerves. Although it is

³ Mahoney and Sheehan (9) found that extirpation of both stellate ganglia, cervical sympathetic trunks, and superior cervical ganglia did not alter the fright reaction in monkeys with denervated ocular muscles.

possible that the blood vessels to facial muscles might receive fibers from neighboring nerves other than those sectioned, there is no such anatomic evidence at present. Furthermore, the severance of the third, fourth, branches of the fifth, and seventh cranial nerves, together with extirpation of the superior cervical ganglion and sympathetic trunk, should interrupt some of the nerve supply to blood vessels of face or eye, and therefore should have lessened the degree of contraction associated with fright. Not even the slightest diminution in the degree of contraction occurred.

If the fright reaction were not due to a local secretion of acetylcholine, then one might postulate that the parasympathetic humoral substance reached the denervated muscles through the circulation. The fact that Freeman, Phillips and Cannon (11) could not demonstrate acetylcholine in the blood after stimulation of the vagus, as Brinkman and Velde (12) did, in 1925, does not detract from the possibility that during fright or under conditions of strong emotion, where the entire organism is activated, an excess of acetylcholine-like substance is secreted in all parts of the body, such as at endings of autonomic and motor nerves (13), at sympathetic ganglia (14), and perhaps at many other organs, including the adrenals. A part of this excess of acetylcholine, which could not be so rapidly destroyed in the body tissues,⁴ may have escaped into the general circulation and thus reached the sensitized denervated muscle.

The proof that the contractions in denervated muscles induced by fright are strictly related to the physiologic state during fright may be derived from the following observations. A monkey frightened more than once or twice within a short period by one method showed a reduction in degree of contraction after the first fright reaction. The more attempts made to frighten the animal, the less intense became the reaction. It seemed as if the monkey became accustomed to the threats and refused to be fooled. Every time the animal was frightened or surprised by new methods, contractions in the denervated muscles were invariably elicited. The fright reaction appeared to be more intense with sudden fright and effort to escape. For example, when a monkey held in the examiner's hands made a sudden attempt to escape, and after a very short struggle returned to its cage, the contractions in the denervated muscles appeared and these seemed to be much more conspicuous than those obtained by simple threatening. It seemed that strong exercise augmented the fright re-

⁴ That acetylcholine may persist in the body tissues for periods much longer than in the blood stream was inferred from the observations that contractions in denervated facial muscles, induced by acetylcholine injected intramuscularly in an eserinated monkey, lasted sixty times as long as those obtained by intravenous administration. The rate of disappearance of acetylcholine from the tissue depended, in part, on the rate of absorption of acetylcholine by the blood stream, where it is rapidly destroyed. If sufficient amounts of the substance are absorbed by the circulation, however, it is possible to detect its presence in the blood stream, the denervated muscle acting as an indicator.

action. Exercise alone yielded contractions in the denervated muscles of some, but not all, monkeys. Since the element of fear could not be eliminated in animals which were exercised, it could not be stated with any degree of certainty whether exercise alone was responsible for the contractions observed in some of the animals. Furthermore, repeated exercise after the initial fright reaction had no visible effect on the state of denervated muscles. That fear alone could produce contractions in denervated muscles was verified by the following experiment. A blind and hemiplegic monkey, frightened by noise and a jarring of its cage, did not move or exercise but did exhibit contractions in denervated facial muscles.

Irrespective of whether acetylcholine reaches the denervated muscles from a local liberation or through the general circulation, there appears to be cogent evidence that this substance is secreted in the body during fright, the sensitized denervated muscle acting as an indicator of the presence of acetylcholine. Thus, the discharge of a parasympathetic substance is compatible with certain parasympathetic activities which are known to occur during fright, such as defecation, urination, and in some cases, even slowing, rather than quickening, of the pulse. It is suggested, therefore, that during fright there is a general discharge of the autonomic system and a secretion of "adrenergic" and "cholinergic" hormones. These hormones produce their effects in part independently of the autonomic nerve supply, and act on their specific organs. The interaction between the sympathetic and parasympathetic neurohumoral effects influences the body in such a manner as to protect it in time of emergency. It is probable that there are other humoral secretions which occur during fright but these are not demonstrable, as yet. The contraction of a paralyzed striated muscle during fright illustrates the parasympathetic action in body defense mechanism.

Additional observations made on these animals revealed that humoral control of body processes was found to vary with different animals in the mammalian scale. Using the monkey, mangabey, baboon, and chimpanzee as examples, it was found that the higher the animal in the phylogenetic scale, the less conspicuous were the contractions in the denervated muscles induced by fright or those reproduced by acetylcholine. In connection with these experiments is the well known fact that animals like the cat, frog, and leech possess an increasing predisposition to effects by acetylcholine, the animal lowest of these in the phylogenetic scale being the most sensitive. These experiments seem to support the view hinted by Dale (15) in a Harvey lecture that chemical transmission and hormonal control of the body are primitive and archaic processes.

SUMMARY

Experimental evidence is offered to show that a parasympathetic hormone is secreted during fright. The secretion of this hormone caused

paralyzed muscles to contract, a phenomenon which illustrates one of the many mechanisms of body defense. The interaction between this hormone and the well established sympathetic hormone influences the body in such a manner as to protect it in time of emergency.

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XANTHOMATOSIS (LIPOID HISTIOCYTOSIS) OF THE SPINE

REPORT OF A CASE SHOWING SPINAL CORD COMPRESSION

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The recent interest in xanthomatosis is attested by the plethora of reports dealing with the Schüller-Christian syndrome. This disease, described by Hand (1), Schüller (2), Christian (3), and others, was first thought of in terms of a characteristic triad of signs: defects in membranous bones of the skull, exophthalmos, and diabetes insipidus. Other occasional abnormalities reported in association with these signs are gingivitis (4), falling out of teeth (4), changes in optic discs (4), hypogenitalism (5), skin lesions (6), defects in other bones (7), and scattered neurologic signs (8). In 1924 Berkheiser (9), reporting the case of a girl who showed exophthalmos, nycturia, and changes in the bones of the skull, stated that biopsy showed the tumor to be a xanthoma. The xanthomatous structure of the tissue found in the areas of osteoclasia is now recognized as pathognomonic of this disease. Xanthomatous tissue contains lipoid material, usually cholesterol, and has for its most distinguishing characteristic, foam cells, although cells representing inflammatory and fibrotic reactions are usually present. Recently Chiari (10), and also Davison (11), have reported the presence of typical foam cells in demyelinated plaques of cerebral tissue found in this disease.

The recognition of the lipoid nature of the granulomatous tissue in this disease has led to the discovery of associated lipoid deposits elsewhere in the body in many cases and has led to the interpretation of this disease as a systemic anomaly of lipoid metabolism, related to Gaucher's disease, Niemann-Pick's disease, and amaurotic family idiocy.

With greater delineation of the histopathologic structure and clinical nature of the granulomatous tissue found in the Schüller-Christian syndrome it has become necessary to revise our conception of the gamut of xanthomatosis. We now recognize many variants of this disease ranging from the typical Schüller-Christian syndrome with the usual triad of signs to atypical forms having none of these. It is likely that many cases formerly regarded as multiple myelomata, particularly those involving the lumbar vertebrae, really belong in the general category of xanthomatosis. Gilmore (12) reported the case of a girl one year old, who had exophthalmos and multiple myelomata with collapse of the second lumbar vertebra. Rowland (13) described the case of a boy, three years of age who showed

gingivitis, falling out of teeth, and changes in the bones of the skull. At necropsy this boy showed yellow nodules in most of the organs and also in the body of the first lumbar vertebra. Snapper and Parisel (14) reported a case showing generalized xanthomatosis of the bones with osteoporotic lesions but without associated exophthalmos or diabetes insipidus. Microscopic examination showed definite lipid granulomatosis, with great accumulations of foam cells loaded with double refracting lipoids and fat. Schroff (15) reported the case of a young woman, twenty-three years of age, who showed extensive destruction of the mandible with an associated pathologic fracture of the jaw. There were no other bony lesions and no evidence of cranial involvement. A study of the tissue removed from the area of destruction revealed typical xanthomatosis. Bahls (16) reported the case of a man, twenty-six years of age who showed a solitary cyst in the right humerus without other involvement. Here, too, the tissue was reported as a xanthoma.

Chemical studies have confirmed the belief that xanthomatous lesions found in extracranial areas of osteoporosis and the lesions of membranous bones found in the Schüller-Christian syndrome represent the same fundamental pathologic process. Cowie and Magee (17) studied the total lipid content, phospholipoids and cholesterol in xanthomatous tissue removed from the proximal end of a femur, and from the orbital and temporal region, in a case of generalized xanthomatosis. The quantitative parallelism of their findings was striking.

Invasion of the extradural space of the brain by xanthomatous tissue with adherence to the dura is a common finding in the Schüller-Christian syndrome. Invasion of the spinal extradural space by xanthomatous tissue is a much more unusual finding. Grünwald (18) reported the case of a man with a level lesion of the spinal cord. Radiographic examination revealed destruction of several vertebrae but because of the history of preceding apical tuberculosis a diagnosis of Pott's disease was made and a plaster cast was applied. Because of his failure to improve he was eventually operated upon and a large xanthoma was found in the vertebrae and the extradural space. Removal of the tumor was followed by complete recovery. The patient also presented bilateral exophthalmos. No other cranial anomalies were noted.

Sossman (4), in an important contribution to the therapy of this disease, summarized his experiences with five cases of xanthomatosis and indicated the value of deep X-ray therapy to areas of osteoclasia in the skull. Irradiation of the involved areas in his cases was followed very definitely by healing and regeneration of bone.

The following case, resembling the one reported by Grünwald, is reported as another example of spinal xanthomatosis with massive cord compression, an unusual clinical variant of the Schüller-Christian syndrome.

CASE REPORT

History. R. A., an unmarried colored female, eighteen years of age, was admitted to Grasslands Hospital on August 17, 1932. Her family history and past history revealed no information pertinent to her present illness. She complained of increasing weakness of both lower extremities for twenty-five months. Twenty-one months prior to admission she had resorted to the use of crutches. One year prior to admission she had developed incontinence of urine with increasing dysuria. She complained of occasional twitching of the muscles of the left lower extremity,



FIG. 1. Roentgenogram of the lumbar spine. Note the expansion of the transverse process and destruction of the body of the first lumbar vertebra. A suggestion of involvement of the 12th dorsal vertebra may also be seen.

inconstant pain in her back, legs and feet, and numbness below the waist. She had lost six pounds during the previous two years.

Examination. The patient was well developed and well nourished. The extra-neural physical examination revealed only some carious teeth. She was afebrile. Upon neurologic examination she showed the following: her speech was normal; the pupils were round, regular, equal and responded well to light and in accommodation. The fundi were normal and the other cranial nerves also showed no abnormalities. The tendon reflexes of the upper extremities were lively and equal; there was no ataxia or sensory disturbance in the upper extremities; the abdominal reflexes were equal in all quadrants. There was diffuse atrophy of both legs and thighs.

She showed a spastic paraparesis, and was unable to walk or stand without assistance. No fibrillations or other involuntary movements were seen. There was no muscle tenderness or irritability. The suprapatellar jerks, the patellar reflexes, the hamstring reflexes and the ankle jerks were not elicited on either side. There was no response to plantar stimulation of either foot. There was almost complete loss of perception of pain, touch and temperature bilaterally below dermatome L5 and only mild involvement from L1 to L5. All modalities of sensation were perceived normally above dermatome L1. Posterior column sensation in the toes was impaired, but not completely lost. She was incontinent of urine and feces. Mentally, she was somewhat dull and stolid and showed no overt abnormalities.

Laboratory Data. The Wassermann tests of the blood and cerebrospinal fluid gave negative results. The spinal fluid taken on admission showed 11 white blood

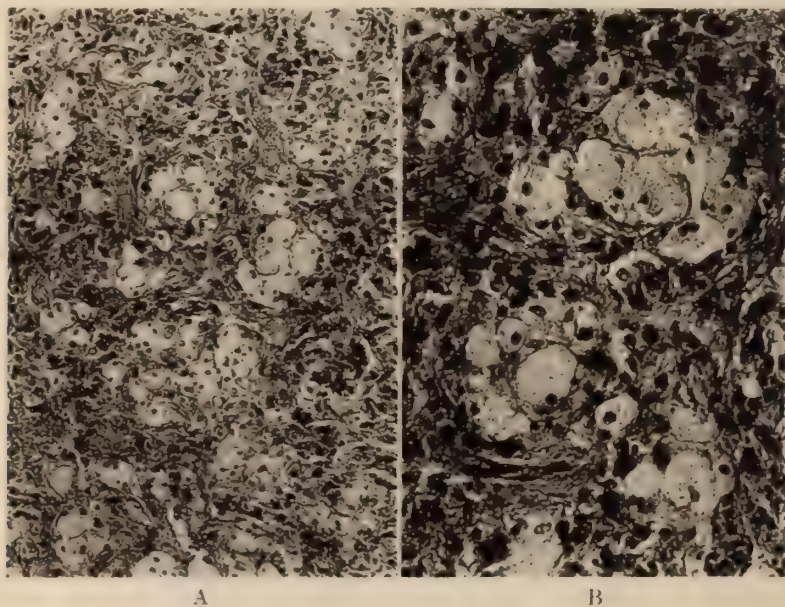


FIG. 2A. Section of the tumor showing characteristic foam cells. Hematoxylin-eosin stain. ($\times 200$)

FIG. 2B. Same as Fig. 2A. ($\times 400$)

corpuscles per cu. mm., 4 plus globulin, and a colloidal gold curve of 1233444444. Two weeks later lumbar puncture yielded only 1.0 c.c. of xanthochromic fluid by spontaneous flow. Not until jugular pressure and coughing were resorted to was the flow increased. The xanthochromic spinal fluid showed six cells, 4 plus globulin, 4 plus albumin, and a colloidal gold curve of 5555555555. The urine repeatedly showed a trace of albumin and some pus cells.

Radiographic examination of the lumbar spine showed an expansion of the right transverse process of the first lumbar vertebra, destruction of the right lamina and pedicle, and destruction of the posterior portion of the body. There was a suggestion of involvement of the 12th dorsal vertebra (Fig. 1). Radiographic examination of the chest, skull and long bones showed no abnormalities.

Operation. The patient was operated upon on September 10, 1932. The spines

and laminae of vertebrae D12, L1 and L2 were removed, revealing a mass of soft, pearly-colored, translucent, and rather avascular tissue. The tumor tissue was entirely extradural, and was found within all of the vertebrae from D12 to L3, invading most of the spines and laminae. The dural sac was found pushed well to the left and the nerve roots within the dura were felt to be greatly compressed. It appeared impossible to remove the tumor mass completely. Only that part of the tumor could be excised which lay dorsal to the dura and somewhat to the right of it. Some of the remaining tumor was curetted away but about three-fourths of the entire mass was not accessible. The subdural space was opened only in one area where the dura was removed accidentally with a piece of overlying lamina. The arachnoid was not opened.

Pathologic Examination. Examination of the tumor disclosed a cellular, actively growing tissue in which little of the normal bone or marrow remnants could be identified. The cellular activity was due to a great increase in myeloid cells, and particularly plasma cells, which lay in large nests and masses throughout all of the tissue inspected. In many specimens, however, a second type of cell predominated:—a large, pale, foamy, endothelial element, growing in sheets and columns, typical of xanthomatosis, (Figs. 2A and B). In these areas the tissue had an organized character and the vessels were well developed.

Following the recognition of the xanthomatous tissue with its characteristic foam cells, a portion of the tumor was subjected to chemical studies for fats and lipoids according to the method described by Sobotka, Epstein and Lichtenstein (19). The solvents employed were acetone, alcohol, and ether and wherever hot extraction was necessary a soxhlet apparatus was used. The analysis was not carried to the point of absolute identification of the individual lipoids, but was terminated with the recognition of several lipid groupings, as follows:

	<i>Grams per 100.0 grams Dried Tumor Tissue</i>
Neutral Glycerides (fats) and cholesterol.....	9.65
Acetone soluble non-lipoidic material.....	3.10
Lecithin, Cephalin, and Cerebrosides.....	0.71
Alcohol soluble Cerebrosides, and Sphingomyelin.....	0.92
Total Extractibles.....	14.38
Residue.....	85.62

Course. Following the operation the patient regained considerable strength in her lower extremities and after several months was able to walk unaided, but on a broad base and with a waddling gait. The tendon reflexes in the lower extremities returned, first on the left and later on the right. Ankle clonus developed on both sides, more marked on the left. Plantar flexion of the toes returned approximately to normal, but dorsiflexion remained weak bilaterally. Posterior column sensation returned completely in the toes. Touch was slightly diminished below S1 and was moderately diminished from L1 to L5. Pain sense appeared to have improved, and temperature sense remained only slightly diminished. The patient regained considerable sphincteric control. Before discharge she was given a course of deep X-ray therapy to the involved area. On November 31, 1932 an inguinal lymph node was removed for histologic examination. In addition to the usual histologic picture, there were also alterations in the endothelium similar to those seen in the specimen removed from the spine.

Following her discharge from the hospital the patient continued to improve. When seen a year later she still had occasional incontinence of urine and episodes of pain in both feet. She walked with a waddling gait. The cranial nerves were

normal. The deep reflexes in the upper extremities were active and equal. Strength was improved in both lower extremities. The left prepatellar and patellar jerks were more active than those on the right. There was bilateral ankle clonus. The plantar reflexes were normal. There was still some hypalgesia in a saddle area over the buttocks and below the knees.

Two years after the operation the patient was again studied. She showed a waddling, spastic gait on a broad base. The cranial nerves were normal. Strength was adequate in the upper extremities but diminished in the lower extremities. The biceps and triceps jerks were lively and equal. No atrophies or fibrillations were seen. The left abdominal reflexes were lively. On the right side the upper abdominal reflex was diminished and the lower was not elicited. The left knee jerk was more active than the right. Ankle clonus was present bilaterally. The lower extremities were slightly paretic and spastic. Plantar stimulation on the left elicited an equivocal Babinski response. There was mild hypalgesia below D10 bilaterally, but light touch was impaired only in the lower sacral segments. Vibratory sense was perceived on both sides but slightly diminished. She showed occasional defects in position sense of the toes. Neither liver nor spleen was palpable. The blood pressure was 134 systolic and 75 diastolic. Pelvic examination revealed that the patient was now several months pregnant. Examination of the preprandial blood revealed a cholesterol content of 200 mg. per 100 c.c., sugar 74.0 mg. per 100 c.c., creatinin 1.3 mg. per 100 c.c., and non-protein nitrogen 24.0 mg. per 100 c.c. Examination of the urine showed 2 plus albumin and pus cells. The blood count was normal. Lumbar puncture was attempted several times but no fluid could be obtained. Cisternal puncture elicited clear fluid, no cells, one plus globulin, and a colloidal gold curve of 1233221000.

Radiography of the patient's entire osseous system revealed no new evidence of destruction of bone. It was felt that further deep X-ray therapy directed to the lumbosacral region was indicated, but it was deemed advisable to defer irradiation until after the termination of the pregnancy, and the patient was again discharged from the hospital. Six weeks later the patient was delivered of a still-born child.

This patient has now received several courses of deep X-ray therapy over the spine and has been under observation during a postoperative period of five years. Her disease appears arrested approximately at the postoperative status. Repeated radiographic studies have revealed no new lesions in the spine, and no evidence of osteoclasia in the skull or other bones. In spite of repeated courses of deep X-ray therapy, no osteogenesis in the involved areas, detectable by radiography, has occurred. She has developed no diabetes insipidus and no exophthalmos. Studies of blood cholesterol, basal metabolism, blood count and blood chemistry continue to show normal results.

SUMMARY

1. A case of spinal xanthomatosis in a colored female is reported.
2. This case is noteworthy because of the extensive destruction of the spine and massive invasion of the extradural space with cord compression.
3. Spinal compression gave rise to the only symptoms for which this patient sought relief.
4. No cranial lesions have been discovered.
5. Evidence of xanthomatosis was found in an excised lymph node.
6. Deep X-ray therapy has effected no detectable regeneration of bone in the spine.

I wish to thank Dr. Gilbert Dalldorf, Director of Laboratories of Grasslands Hospital, for permission to use the histopathologic and chemical data in this case. The chemical studies were carried out by Prof. Wm. C. MacTavish.

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STUDIES IN THE PHYSIOLOGY OF FORCED GRASPING

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Forced grasping is a well accepted clinical phenomenon. Its appearance has been established as indicative of a lesion in the premotor area. Clinically, its importance is minimized by its infrequency. Physiologically, however, the sign assumes much greater importance. It is a symptom of the borderland between psyche and soma. Walshe and Robertson (1) state that "the phenomena included under the various headings of 'tonic innervation,' 'the grasp reflex,' 'forced grasping and groping,' and the like are found to be capable of analysis into two distinct and separable components, the one volitional and the other reflex. The first, the volitional component, includes grasping movements of the fingers, with which movements of the hand and arm through space are sometimes associated. . . . They are in fact volitional movements occurring in individuals whose psychomotor functions have been reduced by disease of the brain to the production of the 'least voluntary' and most 'automatic' movements. They are not 'forced' or involuntary. The second, the reflex component, consists in the tonic innervation of muscles when, and only when, these are subjected to the proprioceptive stimulus of stretch." Concerning the relationship of these components they further state "The grasp is only the local expression of a more widespread mode of innervation of the muscles, and is in this sense a fortuitous phenomenon that does not necessarily provide any clue as to the origin or significance of tonic innervation. For this reason the term "grasp reflex" is undesirable as conveying a false emphasis upon what is no more than a local manifestation. . . . The experimental studies of grasping phenomena in so far as they throw any light upon the problem considered in this paper, suggest that tonic innervation is a true proprioceptive tonic reflex, of which grasping movements are an uncertain concomitant."

The introduction of the concepts of "volitional" and "involuntary" by these authors, as applied to the phenomena associated with grasping, adds little to the elucidation of these phenomena, and introduces into the subject an essentially philosophic orientation. The difficulties encountered in such an orientation are demonstrated by the authors who, though they state that the grasping movements are neither "forced" nor "involuntary," record the following observations in case 2 of their series: "When the patient is told to keep his fingers still under these conditions, he can do so without difficulty, but when he is distracted the grasping movements resume."

In a study of a series of cases demonstrating grasping responses several observations were noted in patients with "forced grasping" that indicated a more intimate relationship between the grasping movements and tonic innervation than was suggested by Walshe and Robertson. These observations are described in the following case reports:

Case 1. E. F., a white female, aged 48, was admitted to Bellevue Psychiatric Hospital. Her history was not obtainable. The patient appeared chronically ill, older than her years, and presented some acromegaloid features, including a definite hypertrichosis. She lay quietly in bed, was rather hypokinetic and emotionally labile. However, her sensorium was fairly clear. She recognized the examiner and would attempt to conceal her right hand from him as he approached. The retinal vessels were severely diseased, and there were numerous hemorrhages and exudates. There was a right supranuclear facial weakness; the tongue deviated to the right and the speech was slurred. The patient presented a mixed aphasia of moderate severity. There was a marked right hemiparesis; paresis of the left lower limb with atrophy of the leg muscles bilaterally; good power in the left upper extremity. There was generalized hyperreflexia which was more marked on the right side, with a bilateral Hoffman sign; exaggerated Mayer reflex on the right; absent abdominal reflexes, and normal plantar responses. The heart was enlarged; the blood pressure was 290 systolic and 140 diastolic.

Tonic Innervation. The muscles of the right upper extremity, especially the flexors, were unusually sensitive to stretch. If the forearm was passively extended, the biceps became firmly contracted, stood out in relief, and remained that way so long as the stretch was applied. This type of tone was completely absent in the left upper extremity.

Grasping. Typical so-called "forced grasping" could be obtained in the right hand. Grasping was absent in the left hand, except under the conditions to be described. When the observer approached the patient, she would place her left hand on the right forearm in order to prevent the right hand from grasping. If an attempt was made to remove her left hand she resisted such an attempt, but made no effort to grasp with the left hand. When her left hand was forcibly removed from the field and the stimulus was offered to the right hand, the latter invariably grasped. If the patient was permitted, she immediately brought her left hand to the right and opened the fingers with the right hand. If this was not permitted and (1) the stimulus was removed from the grasping hand but held close by it, the right upper extremity began to grope for it, the left meanwhile trying to prevent this; (2) if the grasping right extremity was extended and abducted so as to intensify the grasp reflex in the right hand by stretching all the flexor groups, the left hand ceased its effort to come in, and if, at this time, a stimulus was offered it, grasping resulted. If, while the left hand was grasping, the stimulus was removed from the right hand, the left hand opened despite tension on its flexor tendons. If the stimulus was not removed from the right hand, the left hand spontaneously relaxed after a variable time.

Case 2. E. R., a white male, aged 50, was admitted with a history of sudden onset of weakness in the left lower extremity one week before. The patient lay quietly in bed, practically akinetic. He did not speak unless spoken to, and made no complaints to the nurses when he wet his bed. There was a marked paucity of spontaneous movement. The patient created the impression of being a dull, lethargic individual, but upon mental examination it became evident that he was perfectly clear, well oriented and had an excellent memory for both recent and remote events. He was able to perform difficult calculations with ease, but was quickly fatigued,

after which his attention could be maintained only with great difficulty. During the course of his stay in the hospital the patient became depressed. He said that he heard God's voice telling him, "You're sick. You deserve it. Just lie there. You did it." He attributed his illness to the fact that he violated the alcohol prohibition law. He stated that he thought the doctors were going to kill him and his apprehension toward examination corroborated this fear. The fundi showed hypertensive vascular disease. There was a left supranuclear seventh nerve weakness; and vasomotor changes were present in the left limb. There was a left hemiparesis, marked in the lower extremity and minimal in the upper one. The left lower extremity was held in semiflexion by the hypertonicity of the hamstring muscles. There was unusual sensitivity to stretch of the flexors of both left extremities; clumsiness of the left hand in the performance of skilled movements; a left hyperreflexia, more marked in the upper extremity; absent abdominal reflexes; a relative left Babinski; exaggerated Mayer reflexes, more so on the left; a mild hemisensory syndrome, more marked in the lower extremities. General physical examination revealed an enlarged heart with a hypertension of 220 systolic and 180 diastolic. The serology of both blood and spinal fluid was negative.

Tonic Innervation. This was present in both left extremities and absent in the right. Passive extension of the left elbow was resisted by contraction of the biceps. The resistance persisted as long as there was stretch. If, while the flexor group was so contracted, the elbow was flexed, the muscles rapidly accommodated themselves to the decreased length, the biceps tendon again standing out in relief. This type of tone was brought out in the extensors of the arm by pronating the hand or invoking support reactions which were clearly in evidence and, when this was done, similar tonic reflex changes were observed in the extensor group. In the lower extremity this sensitivity to stretch was present in the flexor muscles of the knee.

Grasping. Left hand. When an object was placed in the left hand, the patient's fingers closed down upon it, the thumb and index finger usually initiating the movements, followed by the digits with varying speed at different examinations. If the patient was asked not to grasp the object he was at times able to prevent the grasp. This ability varied and was least when the left hand had just opened following a previous forced grasp. The patient was able to relax the grasp if no tension was made on the flexor tendons of the hand. Once tension was created, however, the patient was unable to extend his fingers until this tension was removed. If an object was placed close to the left hand but not into it and was slowly removed, the upper extremity followed it in a groping fashion (this did not take place when the eyes were closed) and when contact was made with the object it was rapidly grasped and drawn to the body. Groping and grasping became more pronounced if it had been immediately preceded by a forced grasp. When the patient was asked why he grasped, his reply was, "Well, I thought you wanted me to." However, when he was told that this was neither demanded nor expected, he nevertheless continued to do so. If the fingers of the patient's right hand were used as the stimulating object, a grasp did not usually take place even though adequate cutaneous contact was maintained over a period of minutes.

Right Hand. The right hand usually grasped an object that was offered but the nature of the grasp was less stereotyped than that of the left hand. The fingers would manipulate the object until the grasp was satisfactory and could relax it with ease at any time, even when tension was made on the flexor tendons. However, if while a forced grasp was being elicited in the left hand, an object was inserted into the right, grasping took place immediately and was maintained as long as the left hand grasped, relaxing when the left hand relaxed.

Sucking Response. When an object was brought to the mouth, pouting occurred, though there were no actual sucking movements. This response was more constant and pronounced during forced grasping.

DISCUSSION

In the cases described it was observed that tension of the flexor tendons of the fingers in the hand with "forced grasping" were associated with the following phenomena:

1. *The transportation of the grasp:* Dr. Paul Schilder called to my attention the observation that if "forced grasping" was induced in the affected hand, grasping could then also be obtained in the normal hand, even if previously unobtainable in this hand. This occurred only when the flexor tendons of the affected hand were stretched, the grasping in the normal hand usually enduring as long as the tension was maintained. This phenomenon was noted in both cases. In case 1 it was accompanied by a rather dramatic alteration of the patient's attitude. She was ordinarily irritated by any attempt to elicit the grasp from her affected hand. The patient would protect herself from grasping by the use of her normal left hand. However, when the flexor tendons of the right hand were stretched, her left hand also groped for objects and grasped them when contact with the hand was made. When this stretch was discontinued, the patient was again reluctant to grasp, and again employed her normal left hand to retract the right hand from the observer.

Enhancement of the tonic innervation by stretching the flexor tendons of the fingers of the affected hand was thus associated with the presence of grasping responses in the normal hand when such responses were not otherwise obtainable.

2. *The facilitation of the grasping movement:* Patients with "forced grasping" can frequently inhibit the grasp if a conscious effort is made. This capacity varies from time to time in the same patient. In case 2 the patient was least able, and frequently unable, to inhibit a grasp if it was immediately preceded by a grasp during which the flexor tendons had been stretched.

3. *The relation to the sucking response:* Bieber (2) has observed that grasping and sucking are directly related. In case 2 pouting movements were obtained in response to objects held in front of the patient's mouth. This response was more constant and pronounced during grasping when tension was made on the flexor tendons of the affected hand.

The association of these phenonema with changes in the tonus of limbs manifesting "tonic innervation" suggests that the grasping movements are more than just "an uncertain concomitant" of tonic innervation. Moreover, if grasping movements are considered "volitional movements occurring in individuals whose psychomotor functions have been reduced," they should be bilateral. Usually the grasping movements are predominant on the side of the tonic innervation. In case 1 the involved right hand grasped, the left rejected. The following thesis is offered to explain the relationship between the grasping movements and tonic innervation.

Certain cortical areas (including the premotor), important for the organization of action, must be involved to result in the disturbances seen in "forced grasping." These areas when functioning normally, inhibit grasping responses. They make available to the individual resources capable of instituting an effective and independent adaptation. When the function of these areas is disturbed, the normal organization of action is disturbed. Grasping, previously inhibited by the functioning of these areas, reappears as a support mechanism in establishing a more primitive type of adaptation in which a more intimate relationship of subject and object is secured. This intimate relationship between subject and object prevails during early childhood when the incomplete organization of these cortical areas makes an independent adaptation physiologically impossible. It becomes again evident when these areas are disorganized by disease. At this new level of psychosomatic integration, tonic innervation is to be viewed as the tone assigned to the act of grasping. Schilder (3) has pointed out that tone is not an abstraction but is in the service of action. The fact that grasping disappears when consciousness disappears, and tonic innervation remains, does not establish grasping and tonic innervation as separate phenomena. Fragments of an act may be independently isolated during the disintegration of that act without excluding an integral relationship of these parts in the organized act.

The remaining functioning organization centers attempt to preserve the normal adaptation. There thus co-exist, side by side, two orders of organization. In case 1 the more archaic order is reflected in the uncontrollable grasping of the right hand; the more developed order in the total response of the individual is manifested in her attempt to prevent grasping. Depending on the extent of the involvement of these areas and the state of the intact ones, these two types of organization may compete with one another for dominance to determine the total response of the individual. In case 1 stretching of the flexor tendons of the affected hand was associated with a shifting of dominance from the more developed to the more archaic total response. Ordinarily, this conflict for dominance was revealed in the patient's regarding the grasping as something foreign and apart from herself. In case 2, where the involvement was apparently less severe, an attempt was made to coordinate both orders of organization so as to create a total integrated response. The patient was usually able to inhibit the grasp if this were asked of him. The entire organism participated in the grasping which in this patient took on the appearance of a purposeful movement. It was even rationalized by him in his answer to the question, "Why do you grasp?" when he stated, "I thought you wanted me to." There are thus apparently various methods by which the organism handles this dual state of organization.

SUMMARY

Observations were noted that demonstrated stretching of the flexor tendons of the fingers in the hand with "forced grasping" to be associated with:

1. Transportation of the grasp to the normal hand.
2. Facilitation of the grasp.
3. Facilitation of sucking responses.

A thesis was offered to explain the relationship between tonic innervation, grasping movements and the psychic changes accompanying "forced grasping."

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PRIMARY GENERALIZED MYOSITIS FIBROSA

REPORT OF TWO CASES WITH HISTOPATHOLOGY

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Generalized inflammatory disease of the skeletal muscles, in contrast to the localized forms, is very rare. This fact is striking when one considers the volume of the muscles, their active function, their rich blood supply and their direct exposure to injury. Primary generalized myositis may be classified as follows:

A. Acute and subacute forms.

I. Primary suppurative myositis

II. Non-suppurative forms:

Myositis due to *Trichinella spiralis*

Dermatomyositis

Polymyositis hemorrhagica

Neuromyositis

B. Chronic forms.

Dermatomyositis, chronic type

Myositis ossificans progressiva

Primary generalized myositis fibrosa.

Primary generalized myositis fibrosa is probably the rarest form of generalized myositis. Only eight authentic cases were found in the literature. In this paper, two additional cases are reported, and the characteristics of the syndrome are defined on the basis of the whole series.

CASE REPORTS

Case 1. (adm. 356713). A. M., a 20 year old Jewish white male, was admitted to The Mount Sinai Hospital on the Neurological Service of Dr. Israel Strauss on September 6, 1933, and was discharged on September 21, 1933. His main complaints were stiffness and weakness of the muscles of all limbs for four months.

Familial and Past History. Both parents were alive and well. There was no familial history of neurological or muscular disease, tuberculosis, cancer, kidney or heart disease. One sibling, aged 14 years, was alive and well. The patient was born at full term in Arkansas, and lived there until the age of 9 years, when the family moved to New York City. The infantile diseases included measles, chicken pox, pertussis, and scarletina. At the age of 8 years, his tonsils and adenoids were removed. While living in the south, he suffered from chronic malaria every summer, and received relief from quinine treatment. In the fall of 1928, at the age of 14 years,

he had an acute febrile illness for about three weeks, which was diagnosed as infantile paralysis. This illness resulted in permanent partial weakness of the palate, slight dysphagia, and a nasal voice; there were no other ill effects. He was myopic and had worn corrective lenses for ten years. He had made normal progress at school and had completed one year at the University of Pennsylvania. The patient admitted masturbation since the age of 14, and denied sexual intercourse and venereal infection.

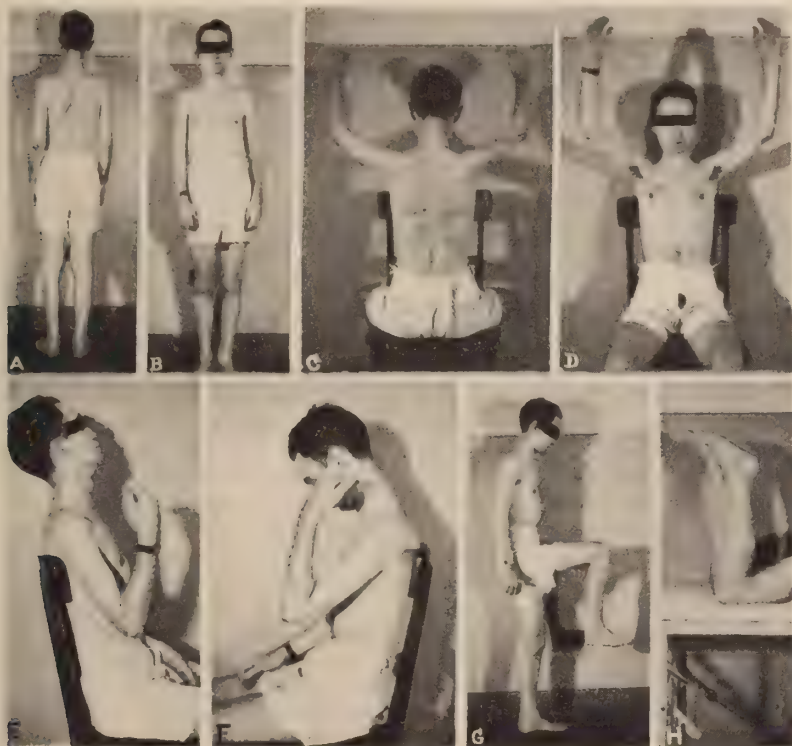


FIG. 1. Illustrations of Case 1 showing the muscular wasting (A and B) and the contractures; patient is trying to raise his arms fully (C and D); to retract his head backwards and to flex his right elbow, wrist and fingers (E); to approximate chin and chest by flexing his neck, and to flex his left elbow, wrist and fingers (F); to flex his right thigh (G); and to flex his knees (H).

Present Illness. The patient claimed that he was in good physical condition until the onset of the present illness. He had passed numerous medical examinations and rowed on the college crew. About five months before admission, he had worked as a dishwasher to supplement his finances. About four months before admission, he noted an aching drawing sensation in his knees. He thought that this was due to lack of exercise, but when he tried to engage in gymnastics he found that his knees became stiffer and that his shoulders were also stiff. He went to camp during the summer and noticed that after exertion, his muscles would stiffen. The aching sensation gradually disappeared. About two months ago, he could not blow on his

bugle as loudly as previously. He then noted weakness in his neck muscles, difficulty in sitting up from a reclining position and weakness in the jaw muscles. The weakness and stiffness had finally become generalized throughout all his muscles, with special involvement of the extremities.

Examination (Fig. 1). The patient was a well developed, but undernourished white male; he was afebrile and did not appear acutely ill. He presented a myopathic facies with broad high cheek bones, depressed nasal bridge, wide upturned nostrils and thick lips. The calvarium was of normal shape and size. The tongue, teeth and pharynx were normal. There was no lymphadenopathy. The chest movements were somewhat limited. The lungs were resonant throughout, and the heart was normal to percussion and auscultation. The pulse rate was 90 per minute and the blood pressure was 135 systolic and 75 diastolic. The abdomen was soft and there were no abnormal palpable masses, tenderness or herniae. The genitalia were normal. Rectal examination revealed good sphincteric tone and the prostate was not enlarged. The skin was dry and thickened, and perspiration was increased. The neurological examination was essentially normal. The fundi were normal except for a myopia of 5 diopters on the right and 3 diopters on the left. The uvula deviated to the right and there was a slightly nasal tone to the voice.

The outstanding symptomatology of the case was noted in the skeletal musculature. The most obvious abnormality was in the hands, where the fingers appeared fixed in a semi-flexed position. Superficially, the hands resembled the deformative ankylotic effects of chronic rheumatoid arthritis. However, when the finger joints were tested, the joint movements were painless, free and unimpaired up to a certain point where further extension or flexion was restricted by the tension of opposing tendons. Similar conditions were found in the shoulders, knees, and hips. It was obvious that the deformity was not due to arthritic changes but to contractures of tendons or muscles. The muscles were not painful or tender to palpation, but when an attempt was made to forcibly move the limb beyond the limit of the contracture, severe pain was induced in the corresponding muscle groups. On palpation, the muscles presented a peculiar hard, firm, inelastic texture. At this examination, the question of loss of muscle volume could not be definitely decided by a number of observers, but in the subsequent course marked atrophic changes became obvious. There was no suggestion of pseudohypertrophy, and fibrillations were not observed. There was definite weakness of all muscle groups. Muscle tone was unimpaired. To a varying degree, all muscles, particularly the large groups, were affected. The masseters were contracted and prevented complete opening of the mouth. The anterior and posterior movements of the head, especially the latter, were limited. On fixation of the scapulae, the arms could be abducted only to about 45 degrees whereupon muscles of the anterior and posterior axillary walls became tense. Complete extension at the elbows was impossible, and supination of the forearms was much impaired. The wrists could not be extended beyond the level of the arm and the flexion movement was limited. The fingers could not be completely flexed or extended, but were active in a restricted in-between phase. The patient showed the typical quadrupedal mode of ascension from the prone position and he was unable to sit up from a reclining position without aid. Sitting down and standing up from a chair were done awkwardly, and could be accomplished only after great effort. Flexion of the back was stiff and partial. The movements of the lower extremities were less restrained, but flexion at both the hip and knee joints were limited. The ankle joints showed the least impairment of motion. Electrical examination of the muscles disclosed definite responses to increased faradic and galvanic currents, and there was no reaction of degeneration.

Laboratory and Other Tests. The routine urine tests were normal. The blood count and hemoglobin were normal and there was no eosinophilia. The Wassermann

reaction in the blood and cerebrospinal fluid was negative. The cerebrospinal fluid was clear, under a pressure of 65 mm. of water; it contained no cells and the total protein was 30 mg. per cent. The blood sugar was 65; urea nitrogen, 20; creatine, 1.2; uric acid, 3.3; cholesterol, 130; calcium, 9.6; and phosphorus, 5.0 mg. per cent. The Janney sugar tolerance curve was normal. Gastric analysis revealed much mucus; the highest total acid was 68, and the highest free hydrochloric acid, 14.

Roentgen examination of the skull showed the sella turcica to be normal in shape and size; there was evidence of some calcification at the insertion of the tentorium on the dorsum sellae. Roentgen examination of the right shoulder, right elbow and right hand failed to reveal any evidence of bone disease. The electrocardiogram was normal. The basal metabolic rate was plus 17 per cent. The dermatological consultant (Dr. M. Scheer) reported: "slight thickening and a violaceous red appearance over the knuckles and dorsal surfaces of the proximal phalanges of both hands; some lichenoid papules on the hands, and upper part of the chest but no lesions either on the mouth or genitals; no evidence of dermatomyositis; the diagnostic impression is either neurodermatitis or lichen planus and this eruption has no relation to the neuromuscular condition." Biopsy of the left pectoralis major muscle was performed; the histological findings are described below with those of Case 2.

Course. The patient received his last follow-up examination in October, 1937. He was much improved but was still considerably disabled. He had completed his course at college and received a B.Sc. degree (economics) in 1935. At present, he is an office worker in his father's place of business and has assumed considerable responsibility. During the past four years, he has received a great variety of treatment including glyocoll, diathermy, physical therapy, calcium gluconate, suprarenal cortex, high vitamin products, and others. The patient and his physician report considerable benefit from glyocoll which he has taken regularly in large doses. The patient states he is able to work, but tires easily towards the end of the day, and has to take a few weeks' rest at regular intervals. Physical examination showed marked generalized muscular atrophies. The muscles had a similar hard firm consistency, there were no fibrillations and marked contractures were still present. The neurological examination was unchanged and essentially negative.

Case 2. S. B., a 34 year old Porto Rican, white female, was admitted for observation to the Psychiatric Division of the Bellevue Hospital from March 13 to March 21, 1934, and again from July 17 to August 4, 1937. On both occasions there was a history of a gradual onset of increasing mental depression and vague persecutory delusions. Other mental symptoms were frequent crying spells, insomnia, loss of appetite, general disinterestedness, inability to concentrate on her work, unsupported ideas of infidelity regarding her husband, and vague fears of being poisoned or attacked by men. She had no hallucinations and no evidences of intellectual deterioration. Following her first admission, she recovered after four months' residence in a State hospital for the mentally sick, and on the last admission, she was again transferred to a State hospital for treatment. Since further reference to her mental condition is not pertinent with this report, only her physical condition will be considered.

Familial and Past History. The patient was indefinite about the details of her past history. No other more reliable informant could be obtained. She was born in Porto Rico. Her mother, one brother and one sister were alive and well. She did not remember her father. Her sister had eight children who were alive and well. There was no familial history of nervous, muscular or mental disease. She had malaria at the age of 10, pleurisy in 1925, and pneumonia and erysipelas in 1928. She had one illegitimate female child, aged 15 years, who was retarded mentally. (Examination of this child showed no systemic, neurological, joint or muscular abnormalities, except for mental deficiency—high grade moron level.) The patient

married ten years ago. In 1931 she had a therapeutic abortion and induction of premature menopause by X-ray.

Present Illness. For the past fifteen years the patient suffered from a disabling condition of her skeletal muscular system. She dated the onset as following the birth of her child, when her whole body became swollen. She denied a skin rash, fever, joint or muscular pains. At about the same time, she noted difficulty in moving her hands, and later contractures of the fingers became evident. A change of climate was advised and she emigrated to the United States. Progressive limitation of motion in all joints with stiffness and moderate weakness gradually occurred. The disability of her hands was the most incapacitating, and walking up and down stairs was difficult. Despite her condition, she continued to attend to her household duties. The degree of her disability varied from time to time, and she claimed that she felt better after walking around or exercising. During the past ten years, she was treated for rheumatoid arthritis for varying intervals in a number of hospitals, with little improvement.

Examination. The patient was a well developed, undernourished white female who was ambulatory, afebrile, and did not appear to be acutely ill. The head was normal in size and shape, and she had a myopathic facies. The tongue was coated. She had a few lower teeth and an upper false denture. The pharynx was normal. The trachea was in the midline, and the thyroid was not enlarged. There was no lymphadenopathy. The breasts were normal. The heart and lungs were normal. The pulse rate was 80 per minute, and the blood pressure was 130 systolic and 90 diastolic. The abdomen was soft and there was no tenderness, hernia, palpable viscera or masses. Pelvic examination was deferred. The skin of the hands was whitish, smooth and atrophic, and perspiration was generally increased. The neurological examination was essentially normal, except for slight hyperreflexia on the left. The gait was somewhat stiff.

The skeletal musculature was obviously atrophic with generalized contractures causing deformity of the joints. Passive or active movements of the joints were free and painless to the limits permitted by the muscle contractures. The muscles were neither painful nor tender to palpation except when stretched beyond the limits of the contractures. As in Case 1, the muscles felt peculiarly hard, firm and inelastic in texture. There were no fibrillations. Muscle tone was good. Considering the marked changes of the muscles, their power was remarkable. Movement at all joints was limited. The masseters were partially contracted. The head could be flexed to approximate the chin and chest, but it could not be extended backwards. The arms moved freely backwards or forwards at the shoulder joints but abduction was arrested at about 30 degrees. The elbow joints showed good movement. The forearms at rest were held in marked pronation and only partial supination was possible. The wrist joints could be flexed easily, but could not be extended beyond a straight line with the arm. At rest, the fingers were in marked flexion, and complete extension and flexion was impossible. The back was rigid and movement of the spine was restricted. To sit up from a reclining position, she had to turn over to the quadrupedal position. Flexion at the hip was limited to about 30 degrees on the right and about 20 degrees on the left. Flexion of the knees was limited more on the right than on the left. The movements of the feet were least affected. Electrical examination of the muscles showed definite responses to faradic and galvanic currents of increased strength, and there was no reaction of degeneration.

Laboratory and Other Tests. The routine urine tests, blood counts and hemoglobin were normal. There was no eosinophilia. The blood Wassermann was negative. Fasting blood sugar was 65 and the glucose tolerance curve was normal. The blood non-protein nitrogen was 25; cholesterol, 160; calcium, 10.8, and phosphorus, 4.1 mg. per cent. The albumin-globulin ratio was 3.9 to 2.6. The basal metabolic rate was

minus 16 and minus 14 per cent. Roentgen examination of the skull was normal. Roentgen examination of the thoracic and lumbosacral spine showed no gross pathological changes. Roentgen examination (Dr. Lewis J. Friedman) of the joints showed mixed atrophic and hypertrophic osteoarthritic changes in all the joints, with flexion deformity at the knees, wrists and hands. The joint changes were

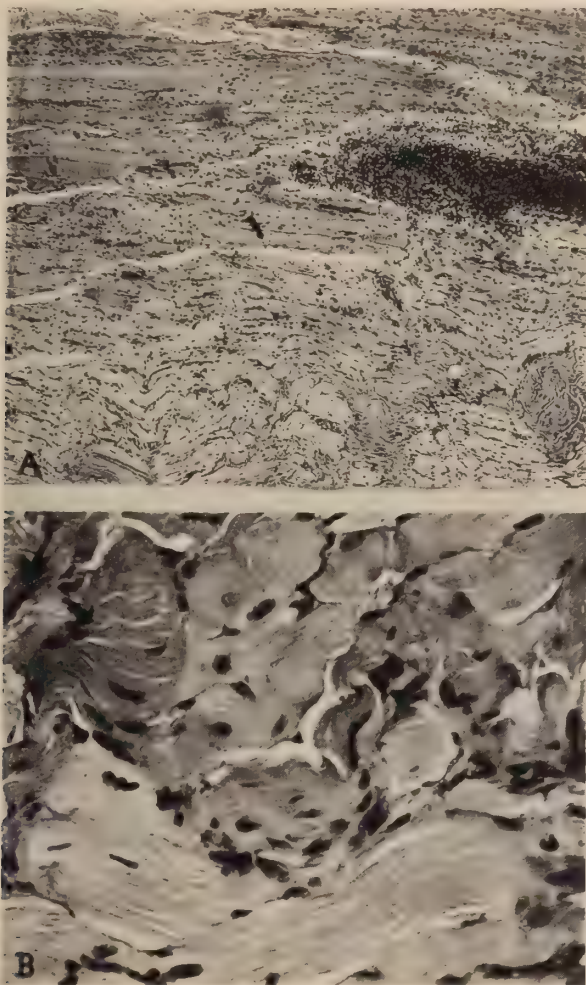


FIG. 2. Microphotographs of the pectoralis major muscle from Case 1 showing muscular degeneration, inflammatory cellular infiltrations and fibrous sclerosis. B is a higher magnification of an area of sclerosis from A.

reported as unlike those observed in rheumatoid arthritis, in view of the fact that there were minimal atrophic changes of the joint extremities and these findings could be secondary to chronic muscular disease.

Course. The patient was treated symptomatically with no improvement of the muscular condition. She was transferred to a State hospital for custodial care and treatment of her mental condition.

Histopathology of the Muscles. Biopsy specimens of the muscles were obtained in case 1 from the left pectoralis major muscle, and in case 2 from the left deltoid muscle. The histopathology¹ of both may be conveniently described together.

The first case (Fig. 2) showed a more subacute reaction. The muscle fibers stained irregularly, were separated by edema in many areas and some fibers were swollen. Degenerative changes, consisting of hyalinization, hydropic vacuolization, and irregular loss of the cross striations, were scattered throughout the section. In

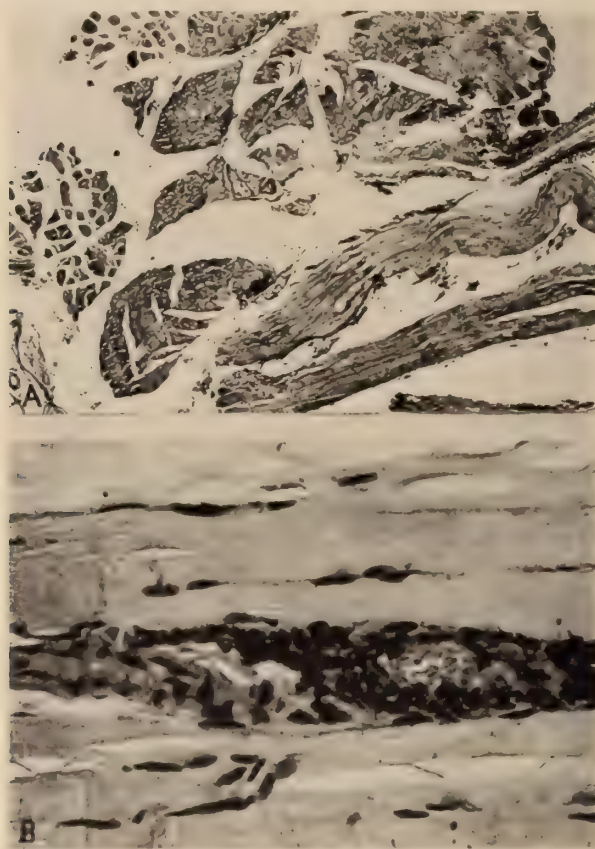


FIG. 3. Microphotographs of deltoid muscle from Case 2 showing (A) muscular degeneration and (B) inflammatory perivascular cellular infiltrations.

many areas, large and small collections of mononuclear cells were interspersed between the muscle fibers. These cells were mainly lymphocytic in type and no polymorphonuclear leucocytes were found. Similar collections of inflammatory cells were also found in the subcutaneous connective tissue overlying the muscle. A third type of reaction consisted of irregular plaques of sclerotic fibrous connective

¹ I am indebted to the pathology departments of The Mount Sinai Hospital (Dr. Paul Klemperer, pathologist) and the Bellevue Hospital (Dr. Douglas Symmers, pathologist) for the microscopic slides of these cases.

tissue. In some areas, the sclerotic reaction was very marked. No hemorrhages or unusual vascular changes were noted.

The deltoid muscle from which the specimen was taken in the second case did not present marked contractures clinically. The histological picture (Fig. 3) showed marked degenerative alterations, occasional inflammatory cellular infiltrations, and very few sclerotic changes. The inflammatory reaction was most marked in the perivascular areas; it consisted mainly of lymphocytes and was generally far less striking than in the first case. The muscle fibers showed considerable vacuolization, loss of substance, fragmentation, and hyalinization. The muscle fibers took the stain irregularly and the cross striations were generally not distinct or completely absent. Many of the muscle cells showed a loss of nuclei.

COMMENT

Typical syndromes of generalized myositis fibrosa are represented by these two cases, which were confirmed by histological examinations of the muscles, and which were seen in the early (subacute) and late (chronic) phases of the disease. Case I was first seen in the subacute phase only a few months after the onset of the disease, and has been followed for four years to the chronic phase. Case 2 is a chronic case with a duration of at least fifteen years. In relation to the few other reports in the literature, both are unique. Burton, Cowan and Fleming (1) have reported the longest follow-up, ten years. The first case is especially significant in that the patient was an adult of superior intelligence who presented an unusually reliable history of the onset of the disease, of his subjective symptoms and of his progress. The onset of the disease would therefore seem to be insidious, and not associated with marked constitutional symptoms or significant pain in the muscles.

Another common feature of questionable significance in these two cases is that both patients had a history of chronic malaria. The level of the fasting blood sugar was low in both cases. The first case had an increased, and the second, decreased basal metabolic rate. Both cases showed a markedly interesting resemblance in the particular muscle groups, and in the amount of incapacitation involved in the final chronic phase. The joints seem to have been fixed more or less in the position which is naturally most frequent, namely: the neck is erect, the elbows are slightly flexed, the forearm is semi-pronated, the wrist is level with the arm, the fingers are semi-flexed, the back is vertical, and the thighs and knees can be bent to a right angle. Furthermore, a striking finding is the active reflexes and remarkably good power despite the extensive muscular atrophy. Both cases perspired excessively and showed atrophic changes of the skin, particularly on the hands. Clinically, the texture of the muscles to palpation was characteristically hard and firm; this has been noted in case reports by other writers.

The histopathological findings in the second case are especially interesting in that foci of cellular infiltrations were present in a case of at least fifteen years' duration. This seems to indicate that the pathological

process is only partially arrested in the chronic phase, and that one may ultimately expect further progression of the condition.

DISCUSSION

Definition. Primary generalized myositis fibrosa is a rare subacute or chronic inflammatory disease of multiple skeletal muscles, which generally begins in the extremities with painless stiffness and slight constitutional symptoms; it leads to early muscular contractures and later atrophies, and is characterized by a peculiar hard firm inelastic texture of the muscles to palpation.

Etiology. Little is known concerning the etiology of this rare disease. Eight cases of primary generalized myositis fibrosa are described in the literature (1 to 9). A few other case reports of myositis fibrosa have been referred to by other writers but these are either localized, atypical, or incomplete. These include the cases of Gies (10), Kreiss (11), and Hoover (12). Jendrassik (13), in his discussion of the myopathies, described a syndrome of muscular atrophy, early contractures and active tendon reflexes, which has points of similarity to the symptom-complex under discussion.

There are no indications of heredo-familial background. One case was that of a negro boy, and the other nine were of the white race. The age of onset of the condition varies from 9 months to 60 years. Both sexes are approximately equally affected. Exposure, exhaustion, debilitating disease, chronic infections and postparturition are mentioned by some writers as predisposing factors. There is no special geographic or climatic incidence. It seems likely that the disease is related pathogenetically to the localized myositides in that the histological picture of the muscle tissue in generalized myositis fibrosa does not differ greatly from that noted in the later stages of other cases of fibrositis. Bacteriological studies of the involved muscles have been negative. Batten (3) suggested the possibility of this condition being allied to myositis ossificans progressiva. Jánossy (14) described myositis fibrosa of the arms as a sequela of gas poisoning. Langmead (15) discussed the relationship of this condition with generalized scleroderma, dermatomyositis and calcinosis. In some instances, generalized myositis fibrosa may represent an end-stage of a special form of dermatomyositis in which the cutaneous complications are fleeting or not very obvious, as in the cases of Gowers (4), Grönberg (7), and Hoover (12). Keil (16), who has made a special study of the cutaneous manifestations of dermatomyositis and related syndromes, is of this opinion. Jendrassik (13) considered the condition as a special type of degenerative myopathy.

Pathology. The disease affects the skeletal striated muscles and shows a preference for the large muscle groups of the upper and lower extremities, and of the back. On gross appearance, the muscles are atrophic, pale in

color and present increased resistance to cutting. Microscopically, there are a variety of degenerative, inflammatory and fibrotic changes. The degenerative changes include irregular loss of striatal markings, hyaline degeneration, hydropic infiltration, and diminution in the size of the fibers. Variable amounts of fibrous tissue are found depending on the extent or age of the disease in the particular muscle. Infiltrations of inflammatory cells in small or large collections are scattered between the muscle fibers. The inflammatory reactions are less marked in the late phases of the disease. The inflammatory cells are mononuclear leucocytes, mainly lymphocytes and fewer plasma cells. The vascular tissues do not show specific changes, and hemorrhages do not occur.

Symptoms. The course of the disease is chronic. The onset is insidious and the early progression is fairly rapid, leading to considerable disturbance of muscle function in a few months. The presenting symptom is usually a feeling of stiffness in the upper or lower extremities, usually the former. As the disease advances, this symptom becomes progressively worse and gradually appears in all the extremities, eventually involving most of the skeletal muscles of the body. In the early subacute phase, the patients become helpless and bed-ridden. The muscles of the face are usually spared, but the masseters are frequently affected. The first objective signs of the disease are the contractures and the resulting limitation of movements. The most marked distortions are evident in the hands where the fingers are more or less fixed in a semi-flexed position. The muscular wasting appears much later than the stiffness and contractures. In many cases, remarkable power is retained despite the extensive disease. Muscular fibrillations do not occur. The tendon and superficial reflexes are usually unimpaired but may be lost in the late stages. Electrical examination of the muscles requires increased faradic and galvanic current, but a reaction of degeneration is not noted.

Considering the pathological changes present in the muscle tissue, it is surprising that pain and tenderness are not more prominent complaints. In the majority of cases, it is entirely absent, and in those in which it is present, it occurs early in the disease and is a minor complaint of short duration. Weakness and loss of weight are the only constitutional symptoms and fever is, as a rule, not observed.

The course of the disease consists of an early subacute period which, in recoverable cases, is followed by a chronic phase. The subacute phase is the most severe and usually incapacitates the individual completely so that he is helplessly bed-ridden. After a few months, there is slow improvement; a chronic condition supercedes, and the patient gradually regains a modicum of muscular function, sufficient for practical needs. In some cases, the disease is progressive without a partial remission, and leads to death from intercurrent disease. In all cases, the chronic period is characterized by variable periods of remissions and exacerbations, and

frequently there is a myasthenic-like reaction at the end of the day. A frequent secondary superimposed condition is atrophic changes of the joints; the joints, however, usually continue to show free movements to the limits permitted by the contractures.

The characteristic texture of the muscles on palpation is an outstanding diagnostic point. To the examining fingers, the muscles feel distinctly harder and less elastic than normal and seem to be increased in consistency. The muscles have been variously described as "hard," "firm," "sandbag-like," "boggy" and "doughy." This distinctive texture of the muscles is present early in the disease before the contracture and atrophies are very noticeable.

Diagnosis. The insidious painless onset of chronic generalized progressive impairment of muscular function, the contractures and atrophies, the characteristic texture of the muscles on palpation, the absence of constitutional symptoms, and the active tendon reflexes constitute a syndrome which should not be difficult to diagnose if this condition is kept in mind. The diagnosis can be confirmed positively by a microscopic examination of a muscle specimen.

A few differential points may be briefly mentioned. The absence of skin lesions differentiates primary myositis fibrosa from the chronic form of dermatomyositis. Amyotrophic lateral sclerosis shows more marked distal atrophies, absent reflexes, Babinski signs, fibrillations, and electrical reactions of degeneration. The muscular dystrophies differ in their familial manifestations, the symmetrical involvement of proximal muscle groups, the pseudo-hypertrophic changes, the predominant weakness, the late minimal contractures, and the early loss of the reflexes. Although the distortions at the joints may at first suggest arthritic disease, this diagnosis is found untenable when the joint movements are carefully examined; the joint movements are then found to be free, painless, and limited only by the muscular contraction rather than by an arthritic change.

Prognosis and Treatment. A consideration of the small number of reported cases does not justify any definite conclusions regarding the outlook. Batten's (3) case died at the age of 6 years after a long duration of the disease, and the case of Schwab, Brindley, Bodansky and Harris (8) died from intercurrent tuberculosis. Other cases, particularly our cases and that of Burton, Cowan and Fleming (1) indicate the possibility of some arrest of the disease process and considerable improvement with restitution of practical function.

Little can be said regarding therapy. The eradication of foci of infection has been suggested on general principles. Physiotherapy in the chronic phase, in the form of massage, gymnastic exercises, and electrotherapy has been beneficial in some cases and seems to be most promising. Most drugs have been of no avail but our case 1 reported considerable

subjective relief of the stiffness by the consistent use of glycooll in large doses. This is interesting in view of the fact that Bodansky, Schwab and Brindley (9) found in their case marked disturbances in the creatine metabolism and in the creatine content of the muscles. The beneficial effects of glycooll in case 1, as has been suggested in other instances of muscle disease with imbalance of creatine metabolism, may be attributed to the building up of the creatine content of the muscles, which is thought to play an important rôle in muscle contraction.

SUMMARY

1. Two cases of primary generalized myositis fibrosa with histopathological studies are reported.

2. The characteristics of the syndrome are discussed and primary generalized myositis fibrosa is defined as a rare subacute or chronic inflammatory disease of multiple skeletal muscles which generally begins in the extremities with painless stiffness and slight constitutional symptoms; it leads to early muscular contractures and later atrophies, and is characterized by a peculiar, hard, firm, inelastic texture of the muscles to palpation.

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CEREBROSPINAL FLUID FISTULA AND MENINGITIS SECONDARY TO FRACTURE OF THE SKULL INVOLVING THE PARA-NASAL SINUSES AND MASTOIDS

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The unusual occurrence of four cases of meningitis secondary to skull fracture within one year, prompted an investigation of the literature dealing with this complication. Three of these cases occurred in a very limited series of head injuries admitted to the Grace Hospital.

An important problem comes up in handling patients with a fracture through the para-nasal or mastoid sinuses, especially when there is clinical evidence that there is a communication between the sinuses and the intracranial cavity. The statistics on the incidence of meningitis in traumatic cases show considerable variation. In a series of 125 cases of frontal sinus fracture reported by Gurdjian (1), only one patient developed meningitis. In only two instances was rhinorrhea present. One of these patients died without evidence of meningitis, and the other recovered without any operative procedure.

Coleman (2) reported eighty-seven cases of fracture of the base of the skull, in forty-nine of which there was free bleeding from one or both ears. Four of these patients died as a result of intracranial infection, giving a mortality of 8.16 per cent. Grant, in the discussion of Coleman's paper, stated that in two years he had seen sixty-three cases in which cerebrospinal fluid escaped from the ear. Only one patient died with meningitis. In five patients he was unable to determine the site of the dural laceration, and no operation was done, with the result that two patients died of meningitis. Teachenor (3) reported ten fatalities from intracranial infection following trauma. These cases were taken from a large series of cranial injuries handled over a three year period. The fracture involved the frontal sinus in six instances, the ethmoid in one, the sphenoid in one, and the mastoid and middle-ear in two. Munro (4) reported one case of meningitis secondary to a fracture through the temporal bone in a series of nine hundred head injuries. He was unable to determine the number of patients who had a temporary flow of cerebrospinal fluid. In one instance, the flow lasted sufficiently long to diagnose a fistula. This patient recovered without surgical intervention. Dandy (5) contributed an article dealing primarily with the question of intracranial pneumatocele, complicating fractures through the sinuses. He collected twenty-five

cases in all, including two of his own. Of this series, six patients died with an intracranial infection.

Table I is an analysis of nine cases of meningitis secondary to skull fracture. These cases were found in the files of two hospitals and represent a part of a small series of head injuries treated over a five year period. In many instances, the patients were not brought to the attention of the neurosurgeon until meningitis had developed. The dural fistula had been closed in only one patient. Sulphanilamide was used in three cases, two of which recovered. Five of the entire group died.

There is considerable variation in opinions regarding the advisability of surgical intervention for cerebrospinal rhinorrhea secondary to a fractured skull. Peet (6) has stated that "whenever a definite diagnosis of a fracture through the cribiform plate can be made, as indicated by the discharge of cerebrospinal fluid from the nose, operation is indicated." Teachenor recommended drilling and drainage of the frontal sinus for those cases in which there has been hemorrhage into the sinus. He felt that this procedure minimizes the danger of infection. Gurdjian was of the opinion that operative interference to curb infection is not needed in the majority of cases. Dandy has stated that cerebrospinal rhinorrhea is not an indication for surgery except in cases of long standing. Munro warned that if a cerebrospinal rhinorrhea is not stopped promptly, meningitis becomes an inevitable certainty. Coleman has written, "the uncertainties as to the location and extent of a fracture of the base involving the sinuses, and the difficulty in the majority of cases of determining the presence of dural laceration, tend naturally to conservative methods in the management of these injuries. Unless there is good reason to believe that an accessible dural laceration exists with communication between the bony sinuses, operation is not advisable." He has exposed the anterior ethmoids a few times to close a laceration of the dura when the spinal fluid leak persisted for three or more days after the injury. With regard to frontal fractures he has said "the frontal sinus may be involved in linear fractures which radiate from the vault and in these cases there is much difference of opinion as to treatment. The majority of such fractures pass through the walls of the frontal sinus to the floor of the anterior fossa and may or may not lacerate the dura covering its inner wall. I know of no way to determine whether the dura is lacerated except by inspection. I have treated such cases conservatively if there was no evidence of infection in the sinus or indications definitely pointing to an hematoma or a leak through the sinus."

Several reports of operative results are available. Teachenor has used the X-ray evidence of fracture and opacity of the frontal sinus as indication for sinus drainage. He recommends removing the posterior sinus wall so as to locate and suture the dural laceration, if rhinorrhea is present or when spinal fluid is found in the sinus. His report consisted of sixteen

TABLE I

	LOCATION OF TRAUMA	PERIOD OF UNCONSCIOUSNESS	CEREBROSPINAL FLUID (CISTULA)	APPEARANCE OF MENINGITES AFTER INJURY	SPINAL FLUID	SIGNS AND SYMPTOMS	TREATMENT	RESULT	POST MORTEM FINDINGS
1	44 Frontal, extending through both the frontal and ethmoid sinuses	12 hours	Spinal fluid from right nostril, first noticed 9 weeks after accident, gram positive cocci in culture	9 weeks	No tap	Impairment of sense of smell, optic atrophy, with marked reduction in visual acuity, loss of peripheral vision in the lower quadrants, and paralytic of upward gaze and slight ptosis of the upper lid on the right side	Semi-sitting posture to encourage drainage until temperature normal and signs of infection gone. Then horizontal recumbent posture, head immobilized with Hauling collar	Working and well 18 months after the injury	
2	12 Frontal, extending into the sinuses	15-30 minutes	None	18 hours	First spinal tap, 18 hours following the accident showed a pressure of 280 and a cell count of 7500 per cu. mm. with 50% polyps. Cultures repeatedly negative	Irrational, Elevated temperature and meningial signs. External rectus weakness and diplopia	Sulphadiazide. Spinal punctures	Entirely well and attending school 3 months after the accident	
3	20 Frontal, extending into the sinuses	15 minutes	Spinal fluid from right nostril	7 days	Non-hemolytic streptococci and pneumococci	Irrational, comatose, elevated temperature and meningial signs. Loss of vision on the right	Repeated spinal punctures. Blood transfusions. Sulphadiazide	Died 16 days after the injury	No autopsy

4	♂	48	Frontal, extending into the right frontal sinus and fracture of the right petrous bone	5 minutes	Spinal fluid from right nostril	11 days	No growth on repeated cultures. Cell count on first specimen 240 per cu.mm. with 50% polys	Irrational, semicomatose. Elevated temperature and meningeal signs. Peripheral facial paralysis, right	Sulphanilamide. Spinal punctures	Well except for headaches and dizziness 4 months after the fall	
5	♂	5	Left petrous bone	From the time of the injury to death	Considerable drainage from left ear	48 hours	Pressure 200, at first puncture. Pneumococcus Type V repeatedly found in cultures	Unconscious, meningeal signs	Spinal punctures, blood transfusions	Died 72 hours after injury	No autopsy
6	♂	20	Compound fracture of frontal bone extending into both frontal sinuses	3 hours	Considerable bleeding from the region overlying the fracture. Question of spinal fluid leak also	48 hours	No spinal puncture	Semi-conscious, irrational. Meningeal signs and elevated temperature	Partial debridement of wound in frontal region. Dura lacerated but not sutured. Wound reopened when signs of infection appeared and irrigated with saline several times daily	Well and able to work as a farm hand several months after the injury. Intermittent drainage from a small sinus tract at the glabella	
7	♂	32	Fracture of the right frontal bone extending into the ethmoid sinus	Several hours	None	72 hours	Pressure 300, cell count 2400 per cu.mm. with 99% polys Meningococci found on repeated cultures	Delirious, semicomatose. Elevated temperature and meningeal signs	Spinal punctures, blood transfusions	Died 9 days after injury	Diffuse suppurative meningitis. Fracture of the right supraorbital plate extending into the ethmoid sinus

TABLE I—*Concluded*

SEX	AGE	LOCATION OF FRACTURE	PERIOD OF UNCONSCIOUSNESS	CEREBROSPINAL FLUID FISTULA	APPEAR- ANCE OF MEN- INGE- TIS AFTER INJURY	SPINAL FLUID	SIGNS AND SYMPTOMS	TREATMENT	RESULT	POST-MORTEM FINDINGS
8	42	Fracture of the left frontal bone involving both tables of the frontal sinus	Several hours	Prolonged drainage from left nostril	24 hours	Spinal fluid analysis 24 hours after admission showed a purulent fluid containing large numbers of streptococci	Relapse into coma, and sharp rise in temperature to 104.5°F.	Blood transfusion, spinal punctures	Died 48 hours after injury	No autopsy
9	41	Compound fracture left frontal region involving both tables of the frontal sinus	Several hours	Nasal bleeding. Question of spinal fluid leak also		No puncture	Relapse into coma and sharp rise in temperature to 105°F.	Blood transfusions. Thorough debridement of laceration in frontal region and site of fracture through the frontal sinus. No tear of the dura in area exposed	Died 4 days after accident	Basilar meningitis. Fracture of the frontal bone. Fracture of the cribriform plate of the ethmoid bone with a laceration of the adjacent dura

cases, divided into two series of eight each. In the first group, there were only three operations and these were done after the onset of complications. There were seven deaths in this first series, two from accompanying brain injury, one from frontal lobe abscess, one from an extradural abscess and meningitis and three from meningitis alone. One patient recovered spontaneously. In the second group, seven patients were operated upon promptly. In one instance, however, the operation was delayed for thirty-six hours and the patient died with meningitis; two patients died of severe brain injury and the other five survived without complications. Munro reported the repair of the dura in three patients with cerebrospinal rhinorrhea with recovery in two cases. Grant in his discussion of Coleman's paper, reported four recoveries in a series of six consecutive cases of compound fracture of the frontal bone with rhinorrhea. No operative intervention has been recommended for cerebrospinal fluid otorrhea.

In this era of rapid transit, traumatic surgery is a very crucial problem, especially since many hospitals along the highways are not equipped for neurosurgical operations and do not have men trained in neurosurgical technique. For the most part, then, a policy of conservatism is in order. There is complete agreement in the opinion that any local therapy to the ear or nose is strictly contraindicated, for the reason that infection may be carried cranialward by any type of manipulation in the ear or nose. If there is no evidence of infection, it is better judgment to discourage the escape of spinal fluid through the fistula by keeping the patient flat in bed with the head immobilized. In the event that infection of the meninges is present, drainage should be encouraged by postural means and by lumbar punctures. Sulphanilamide is an important adjunct where it is definitely indicated. Patients with cerebrospinal rhinorrhea are more likely to develop meningitis than those with otorrhea. The dripping of the spinal fluid over the nasal mucosa irritates these membranes with the result that the patients sneeze. In this way the pressure in the para-nasal sinuses is increased and infected secretions are forced through the rent in the dura. Precautions against coughing and sneezing must be taken. It is imperative to protect the patient with rhinorrhea from upper respiratory infections and strict isolation should be practiced where it is warranted.

SUMMARY

1. A review of the literature on the subject of cerebrospinal fluid fistula and meningitis is presented.
2. Nine cases of meningitis secondary to skull fracture are presented.
3. The treatment of cerebrospinal fluid fistula and of post-traumatic meningitis is discussed.

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GRAPHIC RIGIDITY INDEX

PRELIMINARY REPORT*

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INTRODUCTION

For many years efforts have been made to improve the existing means of treating the sufferers of epidemic encephalitis. The most disabling residual of this disease is the progressive rigidity which leads to incapacity for employment and self-care and is followed by contractures which are often accompanied by pains in muscles and joints.

So many remedies have been tried, so unreliable are the statements of those treated as to the effects of the therapy, and so inadequate are the clinical checks on changes in rigidity, that a serious need exists for the development of some objective method of evaluating the therapeutic results. It was with this consideration in mind, and in the course of treating and studying a group of twenty-five cases of post-encephalitic Parkinson syndrome with massive doses of atropine, that special apparatus was devised by the author to make graphic records of phases of rigidity.¹ These ergographic records of the neck, jaw, hands and feet provided the data which determined the so-called index of rigidity.

Many studies of various phases of rigidity, in animals and man, are reported in the literature, notably those of Pritchard (1), Fukasawa (2), Matzdorff (3), Larnelli and van Bogaert (4), Hawk (5), Manson and Ferguson (6), and Brickner and Lyons (7). Many favorable accounts have also appeared lately, in this country and especially abroad, citing the Römer (8) atropine regime of massive dosage in the treatment of the Parkinsonian syndrome. Among these were reports by Stempler (9), Koenen (10), Adams and Hays (11), Ehrenberg (12), Hall (13), Kleeman (14), Marinesco (15), and Neal (16). However, there is no report available of any attempt to establish objective methods for the accurate measurement of degrees of rigidity, and the changes in them in response to treatment. Owing to the absence of any facilities for gauging and controlling the voluntary motor function in our patients, we did not find it possible to

* Investigations were conducted at the Neurological Institute, Vanderbilt Clinic, and the Physiology Laboratory of the College of Physicians and Surgeons, New York. I am very grateful to Prof. Williams, who extended to me the privilege to work in his laboratory, and who was kind enough to review and correct this paper.

¹ Details of the apparatus and techniques are expected to appear shortly in one of the Bulletins of the Neurological Institute, New York.

measure the amount of extrapyramidal rigidity directly, but through the creation of a standardized formula, derived from the graphic tracings, precise indirect rigidity determinations were made possible.

TECHNIQUE

Graphs are obtained with a Harvard Kymograph, the drum rotating at the rate of one revolution per minute. A single line of the tracing, covering a minute's performance, marked off into five-second intervals, serves as

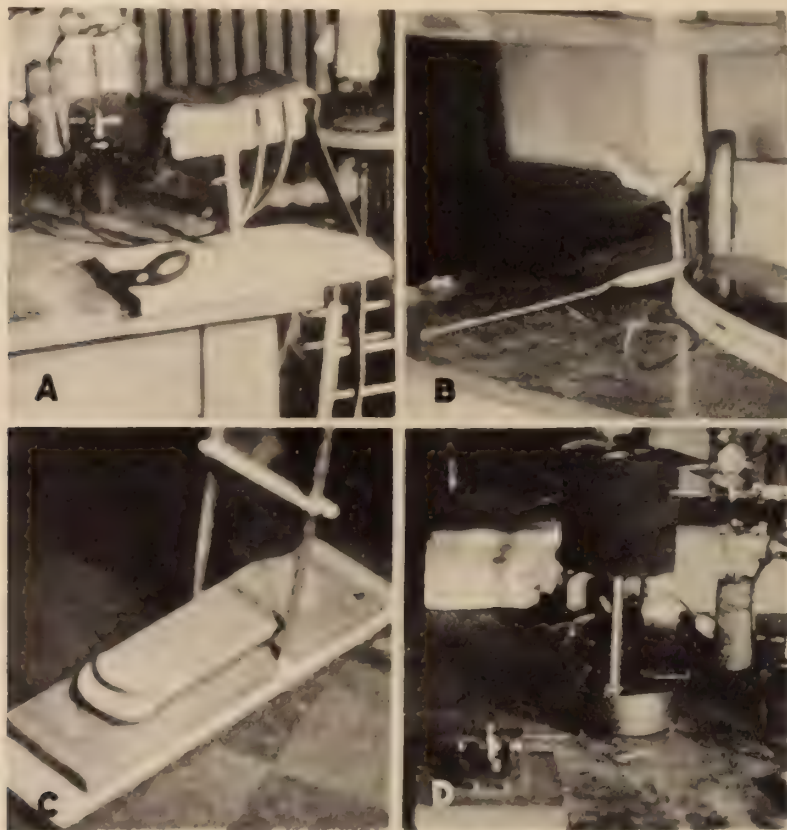


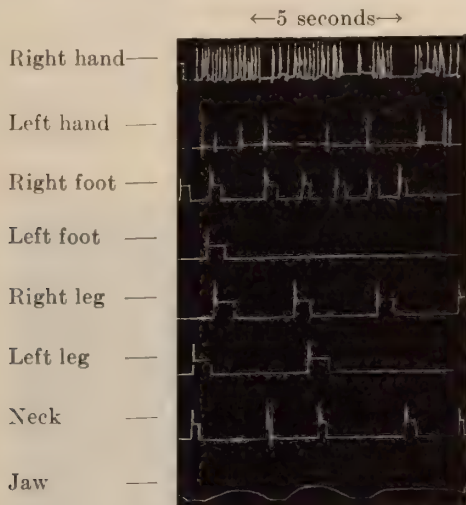
FIG. 1A. Photograph of jaw apparatus with sphygmomanometer cuff. B. Photograph of neck apparatus. C. Photograph of foot and leg apparatus. D. Photograph of hand apparatus.

a record of the function of each part to be tested. To obtain these records, the patient is shifted about a table, on which are located the various forms of apparatus (Fig. 1) specially adapted to test the different parts of the body. In sequence, the frequency, continuity, and amplitude of movement of the right and left hand, right and left foot, neck and jaw are registered on the tracing by these instruments, connected to a signal marker. A two-minute rest is allowed between each test, to prevent the effects of general body fatigue. The graph, when completed, reveals the frequency, regularity, fatigue, and tremors in motor function, all of which

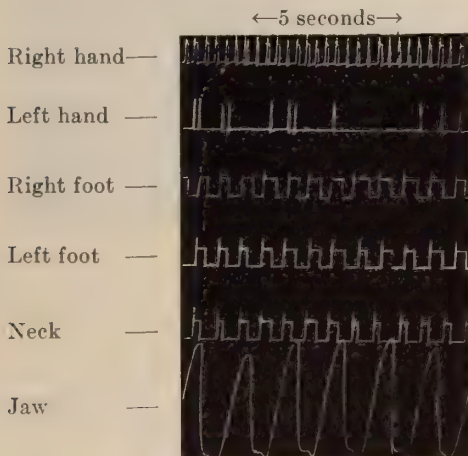
are taken into account in the standardized formula, which establishes the index of rigidity (See Graphs 1a and 2a).

FORMULA FOR THE RIGIDITY INDEX

A study of the graphs of the patients disclosed that certain signs of motor dysfunction regularly presented themselves and these were worked



GRAPH 1a (Case 1). Before treatment 7/10/37

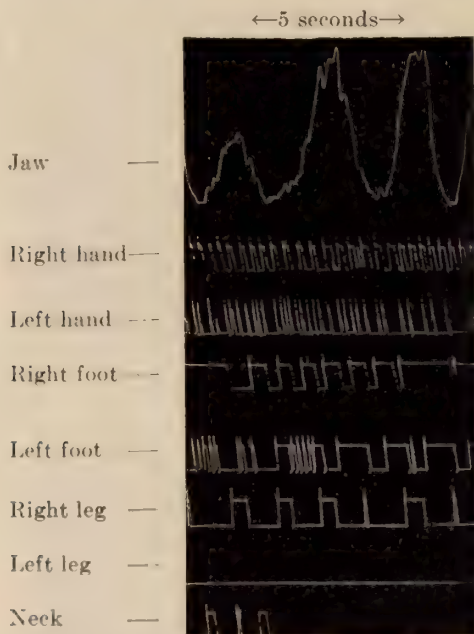


GRAPH 1b (Case 1). After three weeks treatment. Remarkable improvement in performance with neck, jaw and left hand, in comparison with Graph 1a.

into a formula, from which it was possible to calculate the index of rigidity of any part of the body. A rigidity index for the body as a whole was not attempted, since this would be meaningless, in view of the markedly varying conditions existing in the different parts.

There are four elements in the formula, derived as follows:

(A) In the graph of a normal subject (Graph 3), it is observed that the movements of any part are represented on the tracing by contractions of varying width, depending upon the rapidity of performance. At the commencement of each test, the frequency of motion is naturally greater and may register for either hand as many as twenty to thirty or more contractions to a single five-second interval. The five-second interval showing the greatest number of waves on the particular test is called the *best five-second interval*. For either foot, the number of contractions during the best five-second interval of a normal subject may vary from ten to twenty and for the neck and jaw the number may vary from ten to fifteen

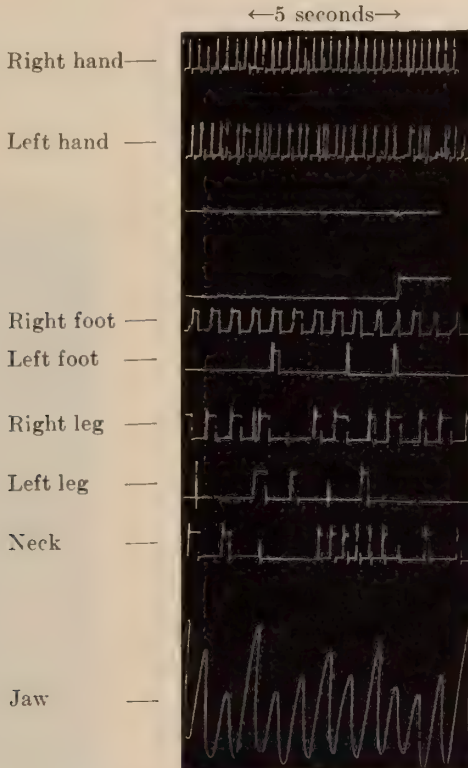


GRAPH 2a (Case 2). Before treatment 3/31/37

or more. In Parkinson cases the frequency during the best five-second interval may be slightly or markedly less, in any or all of the curves for the various parts of the body (Graphs 1a and 2a).

(B) Toward the end of the minute's performance, in any given test, some fatigue appears, which serves to reduce the number of contractions to the five-second intervals, as recorded on the graph. The slowest of these intervals are denoted as the 'poorest five-second intervals.' The average of three of these poorest five-second intervals enters the formula. (See Graph 3). Among Parkinson cases, the fatigue factor, conditioned by pathologic, other than physiologic dynamics, occasions a pronounced slowing down of performance toward the end of the minute in many of the tests.

(C) The difference among normals between the item of best performance and poorest performance is no greater than five contractions, whereas among the hypertonic cases it is almost regularly greater than five contractions, for reasons stated above. This difference accounts for the employment of the *constant of 5* in the denominator of the formula. It helps to demarcate normal motor function, from the abnormal, in the index of rigidity.



GRAPH 2b (Case 2). After three weeks treatment. Remarkable improvement in jaw, neck, right hand and right and left foot performance in comparison with Graph 2a.

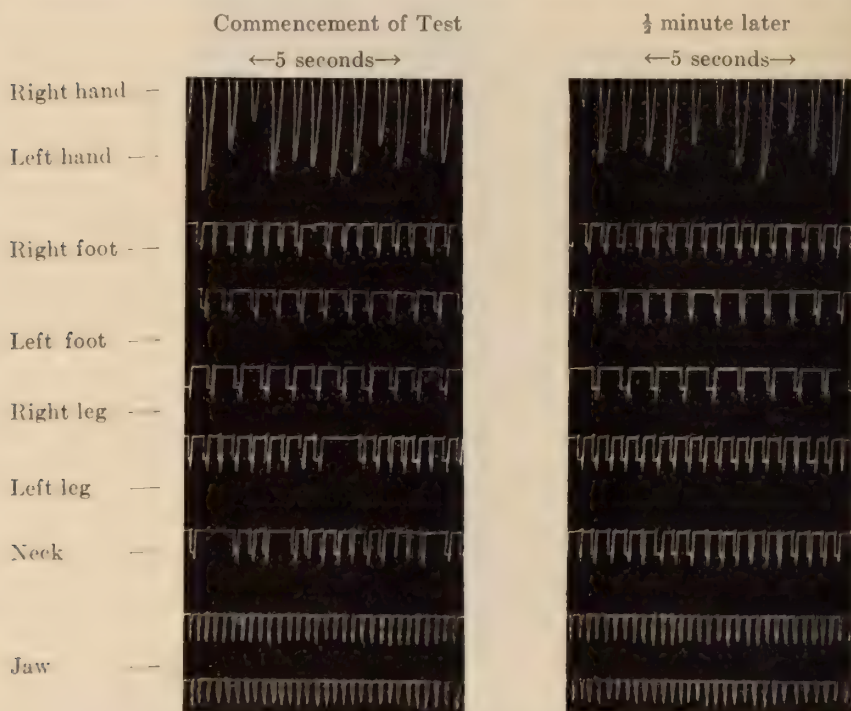
(D) Fatigue reveals itself on the tracings of abnormal subjects, not alone in slowed performance, but also in *rest periods*, any one or several of which may extend from *one to ten seconds* on a particular curve and they may appear in several or all the curves of a patient's graph. They may appear in the tests of both feet and not in the hands, or in one hand and the opposite foot, etc. Our apparatus is not set accurately enough to evaluate *pauses of less than one second*, which may appear also among normals because of momentary distraction or hesitancy; hence these are not considered in the formula. *Rest periods*, however, do not exist on the graphs of normal subjects. The *average of the three longest rest periods*, in

seconds, is entered in the formula to bring out varying degrees of rigidity, for comparison of one case with another, and for recording changes in the same patient at different times, in response to treatment (See curves for left foot of Case 1, in Graphs 1a and 1b).

Incorporating the above elements, the formula for the rigidity index (R.I.) follows:—

$$\text{R.I.} = \frac{A - B}{C \text{ or } 5} + D$$

Under special conditions, two modifications of the formula are employed to account for phases of motor dysfunction, that would otherwise not be



GRAPH 3. Patient M. G. of untreated controls

sufficiently reflected in the index, as in instances of little fatigue and no rest periods, occasioned by a type of slow, steady, plodding performance.

Modification 1 When a limb presents a performance of five or more strokes less than the limb of the opposite side, during the best five-second interval, the difference is added to the numerator of the poorer performing limb.

Modification 2 When the performance of either hand falls below the minimum of fifteen strokes during the best five-second interval, and the foot, neck or jaw below ten, the difference is similarly added to the numerator.

In actual practice the calculation of the rigidity index takes but a minute or two. To illustrate the method of calculation, let us obtain the index of the left foot of Case 1, recorded on Graph 1a.

The best five-second interval (4), less the average of the three poorest intervals (1), leaves a difference (3) in the numerator, to which are added the corrections for the first modification (5), and the second modification (6), making a *total numerator* (14). This *divided by the constant 5* leaves a *quotient* (2.8), to which is *added the average of the three longest rest periods in seconds* (4), making a *final total for the rigidity index (R.I.)* (6.8). Expressed in formula form:—

$$\frac{4 - 1 + 5 + 6}{5} + 4 = \text{R.I. of } 6.8$$

For comparison, let us calculate the index of the same patient's left foot, three weeks later, as recorded on Graph 1b.

The best five-second interval (9), less the average of the three poorest intervals (7), leaves a difference (2), to which are added corrections for the first modification (0) and the second modification (1), making a total numerator (3). Dividing the numerator by the constant 5 leaves a quotient of less than one, and this, added to the average of the three longest rest periods (0), leaves the rigidity index as less than one (−1). Expressed in formula:—

$$\frac{9 - 7 + 0 + 1}{5} + 0 = \text{R.I. of } 0.6 \text{ (expressed as } -1)$$

As this formula has been constructed, normal persons will always have an index of less than one (−1), for evidence of which the reader is referred to Table 3. It is possible for Parkinson cases to obtain a rigidity index of −1 in tests of one or more parts, but this does not signify a total absence of rigidity in the particular parts. In our series of cases, it was regularly found, however, that where the rigidity was sufficient to interfere with function, the rigidity index was strongly positive.

For more rapid calculation of the rigidity index, the following time-saving routine, which includes all the elements in the formula, is employed:—

$$\text{R.I.} = .2(\text{total numerator} + 5 \times \text{rest period in seconds})$$

To calculate the index for the left foot of Case 1 (Graph 1a), with this shorter method:—

$$\text{R.I.} = .2(4 - 1 + 5 + 6 + 20) = .2(34) = 6.8$$

Again, to calculate by means of this rapid routine the index of the left foot (Graph 1b):—

$$\text{R.I.} = .2(9 - 7 + 0 + 1 + 0) = .2(3) = 0.6 \text{ (or } -1)$$

Refinements in the formula and further standardization will be needed, but for the present the formula seems to meet a practical demand. The

matter of evaluating tremor markings on the graph will require further study, as the present practice of counting them at the value of four to one of the normal strokes is not satisfactory.

In the series of Parkinson cases reported here, it was found that, exclusive of the formula, a best score of less than fifteen strokes to the five-second interval for the hand, ten for the foot, and five for the neck and jaw, was indicative of the presence of some degree of rigidity. The index, however, derived from the formula and the two modifications is of far greater service in expressing numerically the progress of the patients under atropine treatment, as shown in Table 1.

RÖMER ATROPINE TREATMENT EVALUATED ON BASIS OF RIGIDITY INDEX

Thus far the writer has been able to check only sixteen of the twenty-five cases on the Römer atropine regime, and these results are presented in Table 1, with the original or basal rigidity scores, the changes obtained in the course of treatment, and the corresponding dates of the graphic studies.

In Table 2 are presented the basal or original indices of the cases that have not as yet been checked.

No treated controls, with forms of medication other than atropine (except those listed in Table 4, on combined atropine and hyoscine, or intermittent atropine and benzedrine), are included in this report, since this does not fundamentally constitute an issue of the present paper.

For purposes of testing the reliability of the formula, the rigidity scores of five normal *untreated* controls are presented below (Table 3), and these uniformly reveal negative indices in all the tests.

Abridged graphs of Cases 1 and 2, appearing in Table 1, are submitted to show the remarkable changes in the patients' performance, after a short period of atropine treatment. A few notes on the histories of Cases 1 and 2 will bring the changes observed in the rigidity indices (Table 1) and in Graphs 1b and 2b, of these patients, into better perspective.

H. P., (Case 1), a 40 year old married man, ill for five years, had been compelled to live away from his family, because of the extreme burden of caring for him and helping him get about. Following three weeks of atropine treatment, he regained sufficient freedom and power in his limbs and body to care for his personal needs, to get about with ease, and to travel great distances to the clinic alone. He has rejoined his family.

E. S., (Case 2), a young unmarried woman of 25, presented an advanced form of Parkinsonism, which had commenced at the age of fourteen. She responded rapidly to atropine treatment, as revealed by rigidity indices, graphs, movies and clinical observations, and returned to active employment, whereas formerly she had been practically in a vegetative state.

A graph of one of the controls is presented for purposes of comparison (Graph 3).

TABLE 1
Checked Cases

CASE	NAME	AGE	DATE	RIGHT HAND	LEFT HAND	RIGHT FOOT	LEFT FOOT	NECK	JAW
Much Improved									
1	H. P.	40	7/10	3.8	5.8	5.	6.8	7.	5.8
			7/31	1.8	4.6	-1	-1	1.8	1.8
2	E. S.	25	3/31	-1	-1	3.8	6.	7.	5.8
			4/21	-1	-1	-1	5.	3.6	-1
			6/4	-1	-1	-1	3.8	2.4	-1
3	S. W.	35	3/10	-1	-1	-1	1.6	1.8	-1
			4/28	-1	-1	-1	-1	1.6	-1
			7/24	-1	-1	-1	-1	-1	-1
4	A. C.	42	1/27	4.4	?	2.2	1.	2.6	-1
			7/31	1.8	-1	-1	-1	-1	-1
5	R. E.	25	2/10	5.4	2.2	5.8	1.8	5.8	4.6
			5/23	-1	-1	3.2	4.4	3.4	1.
6	P. K.	25	3/3	-1	3.6	3.6	4.8	2.2	2.2
			3/31	-1	-1	-1	3.	2.	-1
7	H. F.	34	4/7	1.9	4.8	3.2	3.8	5.2	3.
			7/31	-1	-1	-1	-1	-1	-1
8	W. D.	25	3/3	-1	4.6	-1	2.6	5.8	3.4
			8/10	-1	2.6	-1	2.8	2.4	-1
Slightly Improved									
9	M. B.	45	3/10	2.8	-1	4.8	5.	7.	4.6
			7/24	3.2	3.	1.6	2.4	6.	5.8
10	M. S.	40	6/16	2.6	-1	1.4	-1	-1	-1
			7/31	1.4	-1	1.2	-1	-1	-1
11	R. W.	35	6/16	1.	3.8	-1	6.2	2.2	2.4
			7/31	-1	2.2	-1	5.4	1.8	3.4
12	S. H.	22	3/3	1.8	6.8	7.6	7.2	4.	?
			4/21	1.2	1.4	4.4	3.8	?	-1
			7/31	-1	2.6	9.	7.8	3.6	-1
13	W. T.	30	6/8	9.4	6.	2.8	1.8	4.6	3.2
			6/25	7.	2.2	1.8	-1	2.	1.8
14	A. M.	25	1/14	1.4	1.	-1	1.6	2.	2.2
			8/10	1.	1.2	-1	1.4	-1	2.
Unimproved									
15	D. G.	47	6/1	3.6	-1	2.2	2.4	1.8	-1
			6/18	5.4	2.4	6.6	3.6	1.8	-1
16	B. R.	44	2/16	3.2	4.6	2.4	4.8	?	4.8
			8/21	2.4	4.8	4.4	5.2	3.6	4.2

INTERPRETATION OF RIGIDITY FINDINGS

Although the group of checked atropine cases is admittedly a small one, it nevertheless possesses a certain significance from the fact that the changes are precisely and objectively evaluated. The rigidity index, when further

improved and standardized, should constitute a good laboratory aid to the clinician engaged in treating Parkinson cases, since it is specific and easily determined. The rigidity index, coupled with clinical observation, carries greater value for interpretation, than when used alone. The index possesses usefulness, in that it can supply exact information on the amount

TABLE 2

Unchecked Cases

CASE	NAME	AGE	DATE	RIGHT HAND	LEFT HAND	RIGHT FOOT	LEFT FOOT	NECK	JAW
17	S. L.	34	2/16	3.	-1	3.6	1.	?	1.8
18	S. E.	45	2/3	6.6	3.8	4.6	3.2	7.	5.8
19	S. R.	44	2/3	2.2	1.	3.6	2.	2.	-1
20	T. M.	49	6/12	-1	-1	1.	1.8	-1	-1
21	A. H.	22	7/10	-1	3.8	-1	1.8	-1	-1
22	J. W.	45	7/16	-1	3.1	-1	-1	-1	-1
23	H. G.	46	5/11	-1	1.8	?	?	?	?
24	F. F.	48	4/14	-1	3.2	5.2	2.2	5.6	5.8
25	I. M.	47	4/7	1.	2.4	1.2	2.	3.2	2.2

TABLE 3

Untreated Controls

NAME	AGE	DATE	RIGHT HAND	LEFT HAND	RIGHT FOOT	LEFT FOOT	NECK	JAW
L. D.	40	7/22	-1	-1	-1	-1	-1	-1
J. F.	55	6/19	-1	-1	-1	-1	-1	-1
M. G.	40	7/2	-1	-1	-1	-1	-1	-1
A. C.	28	8/3	-1	-1	-1	-1	-1	-1
G. S.	37	8/7	-1	-1	-1	-1	-1	-1

TABLE 4

Results of Atropine Treatment Based on Indices

	MUCH IMPROVED	SLIGHTLY IMPROVED	UNIMPROVED	TOTAL CASES
Atropine	8	5	1	14
Combined atropine and hyoscine		1		1
Intermittent atropine and benzedrine (tablet and sol.)			1	1
Totals	8	6	2	16

Note: High ratio of improvement with atropine.

of progress made with different types of treatment and varied dosages of drugs.

Tables 4 to 7, derived from the rigidity indices of the checked cases in Table 1, are presented for whatever tendencies they may reveal, or suggest.

Tables 4, 5, 6, and 7 show the marked significance of the rigidity index,

in bringing the results of treatment so precisely into relationship with such factors as the age of the patient, duration of illness, and the amount of atropine dosage, although it is palpably difficult to draw conclusions from so small a group.

TABLE 5
Age in Relation to Result

AGE	MUCH IMPROVED		SLIGHTLY IMPROVED AND UNIMPROVED	
	Cases	Per cent	Cases	Per cent
20 to 35 years.....	6	75	4	50
35 to 50 years.....	2	25	4	50

Note: Some suggestion that younger patients respond better.

TABLE 6
Amount of the 1/2 Per Cent Atropine and Changes in Rigidity

	MUCH IMPROVED	SLIGHTLY IMPROVED	UNIMPROVED
5-10 drops.....	3		1†
10-15 drops.....	4	4‡	
15-20 drops.....	1	1*	
20-25 drops.....		1	1

* Combined with hyoscine.

† Intermittent with other drug.

‡ One patient of this group, who was treated with ten to twelve drops t.i.d., died recently in Virginia. Details are unknown.

Note: While massive dosage is the foundation of this treatment regime, this table indicates that *exceptionally high doses are not needed*.

TABLE 7
Duration of Illness and Outcome of Treatment

	MUCH IMPROVED	SLIGHTLY IMPROVED	UNIMPROVED
3 to 5 years.....	4	1	
5 to 10 years.....	3	4	1
10 + years.....	1	1	1

Note: A shorter duration of illness tends to favor the prospects for response to treatment.

CONCLUSIONS

1. The rigidity index was developed out of a need for objective and specific measurement of changes in post-encephalitic Parkinson cases, under treatment.

2. The rigidity index consists of a formula and two modifications, based upon ergographic tracings of the neck, jaw, hands and feet, obtained through special forms of apparatus devised by the author.

3. The formula and the modifications seem to describe all types of motor dysfunction, tone, power, fatigue and tremor, in a series of twenty-five cases of Parkinsonism. Restudy of sixteen of these showed that atropine in massive doses (Römer method) effected improvement in fourteen.

4. The reliability of the rigidity index is substantiated by normal controls. The index is found to measure precisely what it is intended to measure, and hence should prove a useful laboratory aid in the treatment of hypertonic conditions, although certain improvements in the formula will be necessary.

5. Employment of the rigidity indices makes it possible, even in a small series of checked cases, to gain precise knowledge with regard to the outcomes of atropine treatment, (a) that the shorter the duration of illness, the better the response, (b) that the younger the patient, the better the prospects, and (c) that unusually large doses of atropine are unnecessary.

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TOXIC ENCEPHALOPATHY. COAL TAR DERIVATIVES AS A PROBABLE ETIOLOGICAL FACTOR

REPORT OF THREE CASES WITH NEUROHISTOLOGICAL STUDIES IN TWO

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Harmful effects, or even death, from the use of aspirin (acetylsalicylic acid) alone, or in combination with pyramidon (amidopyrine), are relatively rare in comparison with the vast amount of these drugs consumed directly, or indirectly, in the form of patent medicines.

Balazas (1) observed 753 cases of aspirin poisoning from the years 1923 to 1929, only 4 of which resulted in death. The minimal lethal dose averaged between thirty or forty grams. His pathological reports indicate merely congestion of all organs. Jankovich (2) reports five cases of aspirin poisoning. In his experience the main characteristic pathological lesion is hemorrhage of the mucosa and serosa of the stomach. Hitch's (3) case of fatal poisoning shows, in addition to extensive submucous hemorrhages of the stomach, a noticeable degree of edema of the meninges over the frontal and parietal lobes. Bowman (4) reports an instance of an acute psychosis caused by aspirin, the patient recovering from the psychosis when this drug was withdrawn. Others (5,6) show that small doses of aspirin, as little as five grains, may cause death. In all of the cases reported so far no mention is made of neurohistological findings. The present report deals with the neuropathological and other necropsy findings in two patients who died after ingestion of aspirin, and aspirin and pyramidon, and the clinical features in another who took aspirin in relatively large amounts over a period of years. Although there is no conclusive proof that the pathological lesions or the clinical manifestations were definitely due to these drugs, it is nevertheless considered advisable to record these observations, so that they may be compared with future studies.

CASE REPORTS

Case 1. History (Adm. M.D. 27-2-2). The patient, a 25 year old male, a night editor of a city newspaper, was well until his fatal illness. Three days prior to admission he complained of headache and of feeling chilly. He vomited repeatedly, the vomitus consisting of watery material only. It was said that the only medication he received was twenty grains of aspirin taken at the beginning of the illness. His headache and vomiting increased in severity and he was admitted to the hospital.

The patient, when admitted, was comatose, restless, cyanotic with irregular

respiration. There were present a left internal rectus palsy, a right facial palsy, and embryocardia with imperceptible radial pulse. He declined rapidly in spite of supportive treatment. Slight twitchings of the right arm appeared. He died ten hours after admission.

General Necropsy Findings. The *lungs* showed intense congestion and moderate edema. There was edema of the pleura. The small bronchi were filled with mucus, but they were not inflamed.

The *stomach* showed necrosis of the mucosa and submucosa. The serosa was markedly thickened and infiltrated by numerous round cells. The *lymphatics* were filled with numerous round cells. One of the larger veins contained a purulent thrombus. The *spleen* showed marked congestion with areas of hemorrhage into the tissue. The *kidneys* revealed marked passive congestion. The *liver* revealed

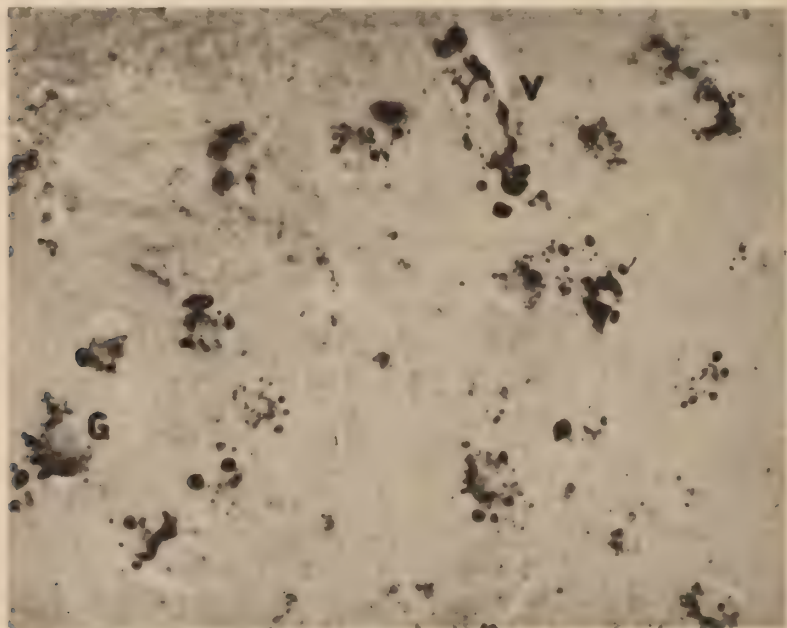


FIG. 1. Fatty infiltration of vessel walls and ganglion cells. V, vessel; G, ganglion cell; Nile Blue stain; $\times 460$.

marked passive congestion and cloudy swelling. The *adrenals* showed passive congestion.

Brain: Gross Anatomy. Upon reflecting the dura, the leptomeninges appeared somewhat edematous. The gyri showed no flattening. There was no evidence of thickening or infiltration of the meninges overlying the left motor area. Particularly near the longitudinal sulcus there were widespread diffuse subpial hemorrhages. Along this sulcus, on both sides, there were a few cartilaginous plaques. The brain was softer than normal. The cranial nerves showed no gross abnormality. The entire brain, particularly the pons and medulla, showed marked congestion. Upon section, numerous spots having the appearance of petechial hemorrhages were noted.

Microscopic Anatomy. The pial vessels were congested. The capillaries were markedly congested and dilated. Perivascular hemorrhages were noted. Perivascular and pericellular dilatation was marked. Areas of rarefaction were noted

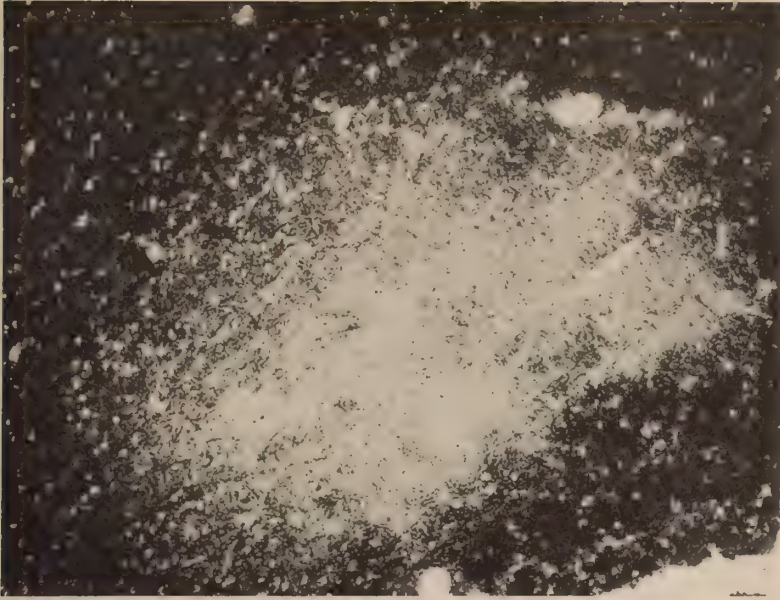


FIG. 2. Area of demyelination in the subcortex. Spielmeyer stain, $\times 100$.

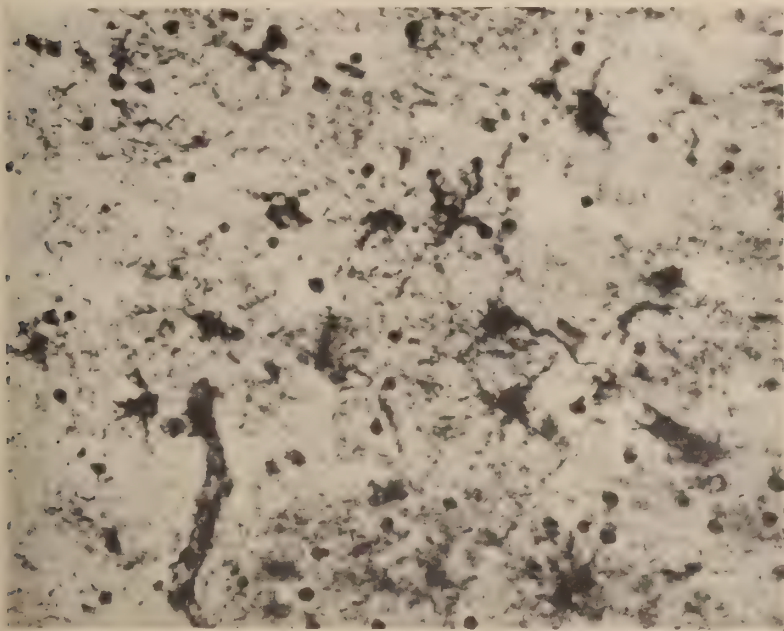


FIG. 3. Clasmotodendrosis of astrocytes. Globus modification of the Cajal stain; $\times 460$.

about some of the vessels. Many of the ganglion cells were in different stages of degeneration; some cells were disintegrated, others swollen; in others the nuclei were eccentric and pyknotic.

The Nile Blue stain revealed many of the vessel walls in the cortex and sub-cortex to be the site of fatty infiltrations. Many of the ganglion cells were similarly affected (Fig. 1).

Areas of demyelination were noted in the subcortex (Fig. 2). Silver stains showed a generalized gliosis. The astrocytes appeared more prominent; they showed thickened bodies and disintegrating processes (clasmotodendrosis) (Fig. 3).

There was no evidence of any inflammatory process in the brain, the lesion having the appearance of a toxic process. Thus, the final diagnosis was toxic encephalopathy.

Chemical Analysis revealed coal tar products present in the body viscera. Aspirin was identified. No other products of forensic interest could be found. The cause of death was given as aspirin or coal tar poisoning with hemorrhages and acute parenchymatous degeneration due to toxemia.

Comment. The neurohistological study of the case of alleged aspirin poisoning reveals a toxic encephalopathy. However, it does not show any changes that can be regarded as pathognomonic of aspirin poisoning. The cause of death in this instance can only be surmised by excluding other factors. The history of taking the drug (aspirin) and its identification after death in the body viscera provide the only evidence for the probable cause of death. The finding of aspirin in the viscera at necropsy throws some doubt on the correctness of the amount of aspirin ingested. It must also be realized that the headache may have been due to some other cause resulting in the encephalopathy.

Case 2. History (Adm. 382703). The patient, a 55 year old woman, had complained of recurrent headache for the past ten years. She had used aspirin and pyramidon frequently and more constantly during the past two years. Two weeks before admission she took two Midol tablets which contained pyramidon (7), in order to relieve headache. A week before admission her headache became exceedingly severe so she took aspirin in a dose much larger than usual. Two days later she was seen by a physician who stated that she had "high blood pressure" and gave her some medication. She immediately began to vomit green colored material. Her throat seemed swollen and she was unable to swallow. She was then admitted to the hospital.

Examination. On admission examination showed: 1) marked lividity of the skin with moderate cyanosis; 2) myotic pupils; 3) shallow ulcerations of the mucous membrane of the mouth, tongue, pharynx, and vagina; 4) crackling râles at the base of both lungs; 5) heart sounds of poor quality in tic-tac rhythm, 136 per minute; radial pulse, imperceptible; 6) tenderness in the left upper quadrant; 7) apprehensive mental state.

The white blood cell count showed only 700 cells per cubic millimeter. There were no granulocytes. The patient was given coramine, intravenous liver extract, and a transfusion of 500 c.c. of blood. She died four hours after admission.

General Necropsy Findings. There were focal necrosis of the liver; parenchymatous degeneration of the liver and kidneys; chronic rheumatic cardiovascular disease; fatty infiltration of the heart; fibromyoma of the uterus; fibroma of the kidneys; hypoplasia of the bone marrow.

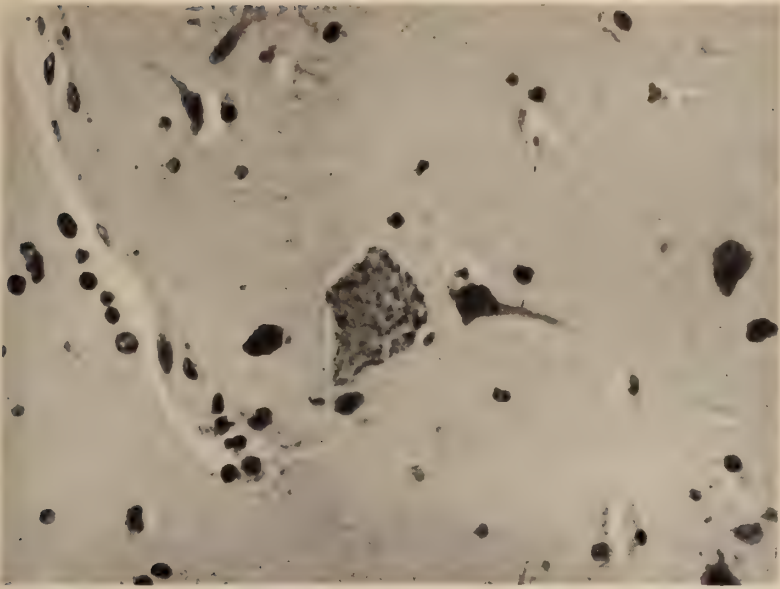


FIG. 4. Ganglion cells in various stages of degeneration. Nissl stain; $\times 460$.



FIG. 5. Fatty infiltration of ganglion cell. G, ganglion cell. Nile Blue stain; $\times 460$.

Brain. Gross Anatomy. In the subarachnoid space over the pons and medulla there was a small amount of bleeding which appeared to be recent, probably agonal. There was slight softening of the right temporal lobe, as compared with the left.

Microscopic Anatomy. The meninges were somewhat thickened. The capillaries were congested. The walls of the arterioles were slightly thickened. Perivascular dilatation was noted.

Most of the ganglion cells were in different stages of degeneration. Some were swollen and undergoing tigrolysis; in others, nuclei were pyknotic and the cell bodies sclerotic (Fig. 4). Perineural edema and neuronophagia were present.

Nile Blue stain revealed the ganglion cells (Fig. 5) and the Purkinje cells to be the site of fatty accumulation. The vessels were affected only to a slight degree.

Silver stains showed a generalized gliosis with marked perivascular mobilization

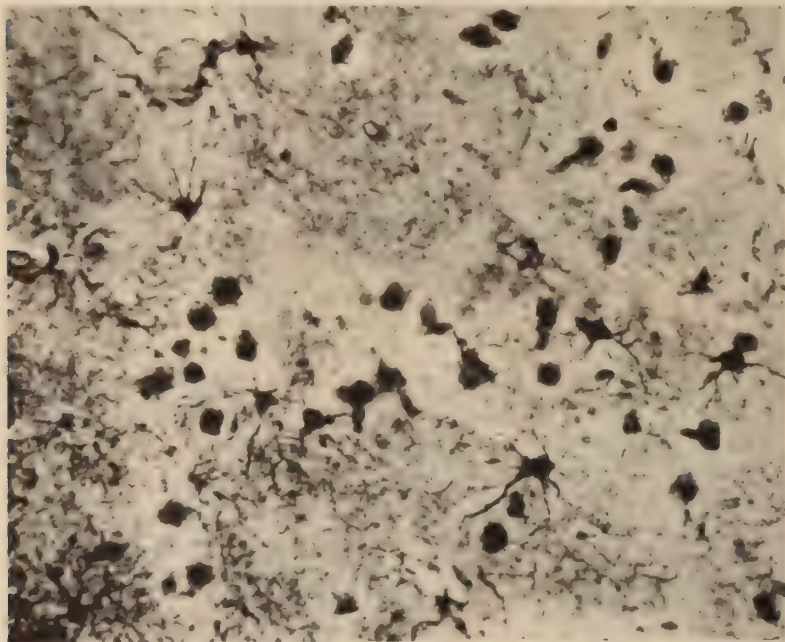


FIG. 6. Generalized astrocytosis. Globus modification of the Cajal stain; $\times 400$.

of the oligodendroglia. The astrocytes were increased in number, but retained a fairly normal structure (Fig. 6).

There was no evidence of any inflammatory process; the cause of death was given as agranulocytic angina.

Comment. This case was complicated by pathological evidence of mild cerebral arteriosclerosis. Therefore, to what extent the encephalopathy was due to the cerebral arteriosclerosis and to what extent it was due to the agranulocytic process, must be a matter of speculation. In 1922 Werner Schultz (8) described a disease entity known as agranulocytosis which later became known as agranulocytic angina. Since then Adams (9) reports over 1,000 cases listed in the literature, whereas Kracke and Parker (7) report over 1,500 deaths in the United States alone in the three year

period ending in 1934. It has been observed that the benzamine group of drugs, such as amidopyrine (pyramidon), phenacetin, acetanilid, arspenamine (9), bismuth and dinitrophenol (10) can cause agranulocytic angina (10, 11). Kracke (12) summarizes the general pathological findings of agranulocytic angina, but no mention is made of the central nervous system being involved. A personal communication from Kracke states that the central nervous system findings are as yet unknown. Norris (13) states that in agranulocytic angina "the cerebrospinal system has been neglected almost entirely, as little work has been reported thereon. There must be changes in the brain that are important as suggested by the weakness and peculiar emotional reactions, such as muttering, delirium, and coma." As in the preceding case, there is no absolute proof which conclusively links the histopathologic findings with the ingestion of pyramidon and aspirin. If, however, the agranulocytic angina was due to the drugs, the findings described assume some significance.

Case 3. History (Adm. 404594). The patient, a 53 year old male, was admitted to the hospital in a state of mental confusion of eight days' duration. Ten years ago he developed a severe migrating rheumatoid arthritis necessitating operations on his feet and right hip joint. He remained relatively well except for arthritic pains which were relieved by aspirin. He consumed fifteen to twenty grains of aspirin daily for the past four years. Five weeks prior to admission he experienced a frontal headache which persisted for one week, and then edema of the entire body occurred. With the finding of albumin in the urine, the local physician made a diagnosis of nephritis. On a milk diet the edema gradually subsided in two weeks. Ten days prior to admission to the hospital it was noted that the patient had an intention tremor of the extremities, which lasted for a few days. His speech was somewhat incoherent and thickened. At times he was confused. He became incontinent of urine.

Examination. On admission, examination revealed a well nourished, middle-aged male. Arthropathies of all the extremities were noted. The blood pressure was 135 systolic and 90 diastolic. The heart and lung examinations were essentially negative. The fundus examination revealed discs of about one-half diopter elevation with a peripapillary zone of grayness, indicative of a pseudoneuritis. On upper convergence, gaze was poor. The abdominal reflexes were absent. The most striking feature was his mental state, which revealed a slight confusion, errors in calculation, a slurred speech and a tendency to grope for a word. He was euphoric but, at times, he became garrulous. When left alone he was drowsy. He was incontinent of urine.

Laboratory Data. Lumbar puncture revealed cerebrospinal fluid under a pressure of 40 millimeters of water. There were 2 lymphocytes per cubic millimeter. The globulin was negative. Blood and spinal serology were negative. The amount of total and free phenols in the urine was within normal limits. The white blood count showed 4,900 white cells per cubic millimeter with a differential count of 74 per cent polymorphonuclear leucocytes.

Course. The diagnosis of a drug psychosis was made and aspirin was considered the cause. The drug was withdrawn and the patient gradually improved, so that on the sixth day the patient was much clearer. He talked connectedly, and was less likely to deviate from the subject. He had good insight into his condition. He

was discharged twelve days after admission, improved. His temperature was never elevated.

Comment. Bowman (4) reported, at the Boston Society of Psychiatry and Neurology in 1933, an instance of a psychosis caused by aspirin. The psychosis was characterized by paranoid delusions and slight confusion. The patient recovered within forty-eight hours after the aspirin was withdrawn, but at a later date the patient insisted her previous delusions were, at the time, true. The discussion that followed revealed the rarity of such an etiological factor of a toxic psychosis. No abnormal neurological signs were given. The case herein described showed, in addition to the psychic manifestations, definite organic neurological evidence of a toxic encephalopathy.

There are two probabilities for the explanation of the aspirin poisoning. The patient at the onset of the frontal headache may have markedly increased his usual dose of aspirin, so that an overdose of the drug occurred. Then again, it is known that therapeutic doses of salicylates may lead to some renal involvement, as shown by the appearance of albumin and casts in the urine (14). Thus the continued use of aspirin over a long period of time may have led to renal irritation, so that the excretion of salicylic acid or salicyluric acid, the end products of aspirin, was reduced.

I wish to express my appreciation to Doctor Joseph H. Globus for his invaluable advice and interest in the preparation of this report.

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NOTES ON A CASE MANIFESTING PARANOID IDEAS

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The purpose of these notes is to record some of the actions, thoughts and conflicts of a patient subject to paranoid ideas and to call attention to the underlying mechanisms. This patient, still under treatment, came under the writer's observation in the early part of 1932 in the Mental Health Class, Out-Patient Department, of The Mount Sinai Hospital. Intensive psychic probing was not attempted as it was not considered safe. One had to be satisfied in managing the situations which arose as a result of the patient's attitude and to discuss material presented by the patient in such a way as to weaken its pathologic momentum. While he was on guard against unwelcome ideas, my attention was also directed to building up the patient's ego by positive accomplishment. Thus this patient, an artist, was able to do good work not only in the free intervals—when he was relatively well, but also to carry on in periods of marked mental upheaval when his work could be regarded only as a form of occupational therapy.

History. The patient, a single man of thirty-eight, presented the following complaints at the initial interview: feelings of doubt about himself, feelings of inferiority and suspicions of the attitude of other people toward him, hostility of others toward him, and a feeling as if constantly at war with his surroundings. The ideas of hostility referred only to men. At one time, the patient was very antagonistic to a former male-friend who had dared to criticize his looks. Feminine company only led to discomfiture and ill-at-ease feeling. He felt that some people considered him homosexual and thought that he had at times actually been approached for homosexual purposes.

The patient was born into a poor artisan family in a small village in Norway. He was the oldest of five children and had three sisters and one brother. As a child he did not make friends easily and tended to keep to himself. He early became an object of ridicule, as the boys nick-named him "boy-girl." He excelled in school work and received a liberal education. His education would ordinarily have procured him office work, but instead, he chose difficult manual labor in the various jobs he held for many years after leaving school.

From early life he paid a great deal of attention to his body. When a mere boy the patient and a friend of his were attracted by a book on Greek sculpture and they developed an ambition to become as beautiful and as strong as marble gods of old. They found a secluded area near the sea where they spent much time building up their bodies through lifting heavy stones, various acrobatic acts, swimming and diving.

At the age of thirty the patient's psychic difficulties became apparent and he began to be tortured by the conviction that people laughed at him and ridiculed him. He

was constantly in fear of being attacked. This fear, at times, was intense enough to force the patient to seek police protection. At the same time he became aware of a strong craving for the attention and company of women. He wanted them to admire his body and looks and resented their admiration of his intelligence. Failure to attract feminine admiration made him concentrate more and more on ways and means of beautifying himself. This, in turn, led to constant humiliation and reproach for engaging in non-masculine activities.

The patient's attention to his body struck a very painful point when he came to feel that the component parts of his body did not follow a single type. He came to look on his reddish hair and fine-featured face as "effeminate" and contrasted them with his masculine large hands and feet. The compulsion for facial care would often drive him into a frenzy, for every blemish had to be eradicated.

As the patient began to search for evidence of masculinity and femininity in his body, physical exercise became a source of pain. This is best expressed in the patient's own words. "I enjoy doing exercise from the toes up to the neck. But when I carry the exercises up to the muscles of the neck and head I am beset with the most dreadful shame and accuse myself of being effeminate. This is really a pity as logically speaking there is no reason why the muscles of the neck and head should be allowed to atrophy." This is quite in contrast with a remark on another occasion. "When complimented about my fine body the compliment leaves me entirely cold. Any cave-man can have a strong fine body, but if one had said something nice about my face it would have been an entirely different matter." There also have been times when the patient felt like cutting his face so as to spoil its feminine appearance. In cooler moments, he has contemplated an operation on his nose to make it look stronger and more masculine.

The manner of his dress also became quite a problem. Wearing a hat was unbearable to him. A remark by the patient, after he became reconciled to the use of a hat, gives a clue to the former basis of this fear. "I put on my hat as though I had always worn one and I thought that I looked quite well in it, I had conquered something. I felt more like a man." He also objected to use of a tie, remarking "Why a tail?" He preferred to wear an open shirt adding "Women do not hide their chests although they have breasts, why should men?" He resorted to many ways and means to hide his large hands and feet. He often wore working clothes on social calls. This he would explain in various ways: the rough working clothes made his big shoes less conspicuous; they helped to preserve his individualism. It did not occur to him, however, that he might thus be trying to put on a masculine front.

Another incident is worthy of note as indicative of the patient's drive to prove his masculinity. In an early fall, when New York suffered a semi-hurricane and people were shivering because of the drop in the temperature, the patient, semi-aware of its import, walked out in the rain to the beach and swam for an hour to prove his manly vigor.

His relationships with women have been limited and short-lived. On one occasion he remarked "I can't love a woman because I love myself." He felt attracted to young girls six or seven years of age. He wanted to caress them and kiss them but he never carried out his desires. The following two dreams showed the same tendency: (1) "I was sitting outside the house, resting, when two young girls came out. They were very attractive and I yearned for them but they walked away. I was again sitting on the same place, but was now dressed in my good clothes. One of the girls came out—she was dark-haired, dusky-eyed and lovely. I possessed hypnotic power which I used to attract the girl. She came and sat in my lap. Using my hypnotic power I secretly commanded the girl to kiss me—she did so. 'You kissed me' I said to her, not without triumph. She smiled, partly embarrassingly

and partly because of her characteristic desire to mystify and conquer." (2) "I was dancing with the older daughter of a friend of mine. She was a sensual girl of eight. She pressed close to me as we danced. I responded and pressed my body close to hers."

He entered into friendship with several adolescent girls. The contrast in age between him and his girl companions became a perplexing problem. It made him more sensitive to the people around him. He felt that the age contrast attracted their attention. In addition, it intensified his sensitiveness about getting older which had become quite marked during the period of observation. Lately he felt triumphant when it dawned upon him that a mature young woman would be a more appropriate companion for him. He considered this new concept so important that he called up the writer to inform him of his discovery.

This patient's clinical course has varied a great deal. Periods of almost normal life have alternated with psychotic or semi-psychotic episodes. The ideas of reference have persisted, with varying degrees of intensity but at no time has there been a tendency to incorporate them into a system of persecution or conspiracy. Neither has there been any evidence of mental deterioration. On the whole, the patient has shown considerable improvement. He is able to do more work, makes more social contacts, and he is gradually gaining better insight into his condition.

DISCUSSION

Freud in his analysis of the Schreber case has formulated an interpretation of the paranoid mechanism. The pivotal point is a homosexual fixation in the psychosexual development of the individual. Briefly, the normal individual goes through the following stages: auto-erotism, narcissism, homosexuality, and heterosexuality. The paranoid individual comes to grief at the narcissistic-homosexual stage. Normally the homosexual tendencies are sublimated into social relationships with the same sex. The narcissistic-homosexual individual gets into difficulties by reversing the sublimations and sexualizing the social tendencies. The paranoid ideas serve as a defense reaction against a homosexual wish-phantasy. It can often be ascertained that the persecutor was once loved and respected. As the social feelings toward the affected person become sexualized they become intolerable, and a transformation of feelings takes place. The following formula has been evolved to demonstrate graphically the development of the paranoid reaction: I love him—I do not love him—I rather hate him—he hates me which justifies my hating him. The mechanism of projection is thus utilized. The affect is changed from love to hate; what should have been felt from within as love is perceived from without as hate.

In addition to repressed homosexuality, Freud also recognized the narcissistic component of paranoia, manifested by the blurring of the dividing line between the self and the environment as shown by the process of projection.

In the case presented, the narcissistic fixation is evident in the patient's constant self observation and self evaluation. His remark "I can't love a woman because I love myself" speaks for itself. He has also carried on a

long battle with a homosexual trend. One can often discern in his conduct a determined effort to prove his masculinity. He gets one hard-labor job after another. He often dresses in a way which tends to accentuate and prove his masculinity. A former male-friend, who criticized his facial appearance bore the brunt of his hate at the onset of his difficulty. This is in accordance with the Freudian finding: "The one who now on account of his persecution is hated and feared, is the one formerly loved and revered." But as the disease progressed the feeling of hate became more diffuse and the patient exclaimed "I hate all humanity, their grinning leering faces as I have seen them all about me all my life."

The division of the patient's body into two parts, masculine and feminine, adds to the interest of this case as it calls further attention to the contents and motives of the patient's psychic difficulties.

The management of the patient on a superficial basis helped him to carry on. Undoubtedly transference of the patient to the writer played a large part in whatever was accomplished in this case. The paranoid person, while being suspicious of some, can develop and maintain a great deal of trust in others. Naturally the transference is always in danger of breaking unexpectedly, since making it a conscious process might cause the patient to interrupt treatment. It is hoped that further treatment may slowly give the patient more and more insight and better adjustment.

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SPELLING DIFFICULTY AND CEREBRAL DOMINANCE*

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Spelling difficulties frequently occur in functional and organic diseases of the brain. These disturbances often result from a general intellectual defect, but there are instances in which a specific disability seems to be involved. Thus errors in spelling are found with a relatively intact intellect in cases of aphasia and related disorders. Orton (1), who studied persistent spelling disability in otherwise intelligent school children, found that such difficulties were apt to occur in naturally left-handed children who had been injudiciously trained to use the right hand in writing. This fact, as well as the association of spelling disturbances with aphasia, suggests the importance of the dominant cerebral hemisphere in the ability to spell correctly. The assumption of such a link is confirmed by a case with spelling difficulties and other disorders, which was studied at The Mount Sinai Hospital.

CASE REPORT

History. (Adm. 420750). A twelve year old schoolgirl was first admitted to The Mount Sinai Hospital in 1935 because of a history of generalized convulsive seizures. She had been in good health until the year before, when it was noticed that she would gaze vacantly into space without responding to questions. Although she had previously made normal progress at school, she seemed to become dull and had difficulty in learning her lessons. She also developed peculiar twitchings in her hands and about two months before admission had a generalized convulsive seizure with loss of consciousness, opisthotonos, cyanosis and frothing at the mouth. A similar attack occurred one month later.

The family history was without significance. The parents were youthful and healthy; there was no consanguinity. There had been a normal pregnancy and delivery. At four months of age, the patient had whooping cough. When she was four years old, her tonsils and adenoids were removed. In the following year she had mumps and subsequently suffered for a while from severe frontal headaches. Measles developed when she was eight years of age.

Examination. There was bitemporal optic atrophy; horizontal nystagmus, more marked on looking to the left, and bilateral pes cavus. The other physical findings were without significance. Laboratory studies revealed no abnormalities.

Course. The patient was subjected to encephalography. The X-ray examination revealed a moderate internal hydrocephalus. The left lateral ventricle was considerably larger than the right but there was no displacement or other abnormality.

* This paper was read before the New York Neurological Society on April 5, 1938.

During a one month stay at the hospital, no generalized seizures occurred, but episodes of peculiar jerky outward movements of the arms were observed. The patient was placed on a luminal regime and discharged with a diagnosis of degenerative disease of the brain, type undetermined.

Readmission to The Mount Sinai Hospital occurred in December, 1937, two years after the previous discharge. During the intervening period, the patient had suffered frequent generalized convulsive seizures. The attacks had taken place almost invariably at night and were not accompanied by any aura or urinary incontinence. On one occasion she bit her tongue.

In recent months new symptoms had appeared. There were sensations of "electric shocks" which the patient could not precisely localize, as they seemed to affect her entire body and which were so painful that she screamed and wept during the attacks. The twitchings of the arms continued and often at such times the patient fell to the ground, sometimes hurting herself. She did not lose consciousness but could not explain her sudden falls. Once this occurred in front of a trolley and she was struck, receiving minor contusions and abrasions.

In addition to her physical complaints, the patient had experienced difficulty in getting along at school. Her teachers thought that she did not pay attention and that she was neglecting her work. When called on to recite, she would just stand without saying a word. Her spelling suffered especially and sometimes her writing could not be deciphered.

During the interval between the first and second admissions, the patient was treated at various times by private physicians. Shortly before her second admission, she was under the care of a psychiatrist who taught her to write with her left hand.

Examination on the second admission showed no change in the physical findings. An encephalogram at this time disclosed no further changes in the ventricles.

Spelling Disturbances. The patient was examined for spelling ability. It was found that when she wrote with the right hand or spelled aloud, she made frequent mistakes, sometimes adding or dropping a letter, but most frequently reversing the order of letters in a word. For example, she might spell mountain, "MOUNTIAN," or house as "HOSUE" (fig. 1). The spelling of a given word might vary on successive occasions; short words were as apt to be misspelled as long words. The same type of error would recur irrespective of whether the patient wrote spontaneously, copied from a book or spelled aloud. However, she could write correctly to dictation if the words were spelled for her. In assembling words from blocks on which letters were printed, there was a good deal of hesitation and rearrangement but usually the final spelling of a word was correct.

Because of a history of early left-handedness, the patient was asked to write with her left hand, with the surprising discovery that she rarely made errors. The occasional mistakes that occurred consisted usually in omission or addition of letters but there was almost no tendency to reverse the letter order (fig. 2).

The patient was able to recognize her own errors, but only with the aid of vision. She readily pointed out her mistakes after she had written down the words and scrutinized them. However, although she sometimes sensed the fact that her verbal spelling was incorrect, she was rarely able to tell in which way she had been mistaken, and in attempting to correct herself orally almost invariably misspelled the same word with different mistakes.

Some words caused especial difficulty. Thus the patient always tended to confuse "quit-quiet-quiet"; she would interchange "there" and "their". Once, in writing to dictation, she spelled "which" as "w-i-h-t-i-e-h". Discussion elicited the fact that the patient had condensed the two words "which" and "witch". These errors did not occur when the words were written with the left hand.

On one occasion, the patient was asked to write simultaneously with both hands.

She was very much confused and said that her left hand was trying to spell in one way and the right another. She persisted, however, and after a few lines developed a convulsive twitching of both arms. When writing simultaneously with both hands, her concentration was turned entirely to the right hand while the left hand appeared to write automatically.

THE MOUNT SINAI HOSPITAL
NEW YORK

We walked to the store and bought
two bottles of milk a loaf of
bread four pounds of apples
and a chocolate cake

The sunshine was warm and
bright as they drove along
the path which led up the
mountain.

I could not believe that these
people really meant what
they said

Richter of the children whom
steal to find their way
across the field where the
house was built

(PLEASE DO NOT WRITE IN THIS SPACE)

FIG. 1. Specimen of handwriting (right hand) showing errors in spelling

THE MOUNT SINAI HOSPITAL
NEW YORK

We walked to the store and bought two bottles
of milk, a loaf of bread and a chocolate
cake

The sunshine was warm on the path
which led up the mountain.

I could not really believe these people
rather of them were in the field where the
house was built

FIG. 2. Specimen of handwriting (left hand) showing ability to spell correctly

In writing the patient showed no tendency to form her letters incorrectly. There was no confusion of individual letters, such as "p" and "q" or "b" and "d" and no unusual facility in mirror-writing could be demonstrated. The handwriting of the right hand showed greater facility than that of the left.

Intellectual Disorders. The intellectual disorders of the patient were not confined

to spelling. In her speech, she occasionally reversed the order of syllables, such as speaking of "Fransancisco" when she meant San Francisco. In taking dictation, she was not infrequently baffled by the sequence of phrases. She would ask, "Did you say come by subway in the morning?" or "come in the morning by subway?" The recollection of names and addresses was an almost impossible task for her. When given such a name as "John Charles Frank, 387 Main St." to remember, she would reproduce every possible combination of these names and numbers but rarely gave a false individual name or number. On the other hand, she did fairly well in immediately repeating word-series or word-pairs given to her.

Historical dates were a source of great despair to her. When asked in what year Columbus discovered America, she replied at different times "1492-1924-1942". The same errors occurred when she wrote the dates with her right hand but she was almost invariably correct when answering the questions by writing with her left hand.

Arithmetic was very confusing for her. She could usually do simple arithmetical processes readily but was perplexed when required to solve problems involving fractions, the relationship of numerator and denominator being too complex for her to grasp. The left hand was of little avail in overcoming this difficulty.

Intelligence. Until recently the patient has been an average student and was graduated from public school a few months ago. She has been unable to attend high school because of illness. The Stanford revision of the Binet-Simon tests showed a mental age of 12 years and 10 months as against a chronological age of 14 years and 1 month. There was a great variation in the performances on this psychological test. The patient revealed superior ability in vocabulary tests, definitions and other performances requiring the ability to handle abstract ideas. Her capacities were very limited, however, when any problems were presented which required arithmetical reasoning or mechanical ability. She could not set the hands of a clock and did poorly in paper-cutting tests.

Other tests given to the patient disclosed further disturbances in the visuo-kineshetic sphere. She failed almost completely on the Kohs block test; she could not cut a star from a piece of paper; she had great difficulty in putting together a few scraps of torn paper. To make a drawing of even the simplest object from memory or from a model was a great problem for her.

When confronted with a difficult task, the patient usually sat motionless for a long time; probably some of these occasions were attacks of petit mal. There was no "trial-and-error" approach. It appeared as though she made no attempt to solve the problem. When asked what she thought of during the long pauses, she would answer "nothing" or "I don't know." However, she was always well-behaved and obedient. It was difficult to secure information from her and in her conversation she was often extremely blocked and retarded. In the Rorschach test, she did not have any association whatever to the pictures; there was a similar difficulty in word-association tests. Specific tasks were carried out more readily than those of a general nature. The patient confided that when called on in school, she could think of the answer a moment before rising and a moment after she sat down again but not during the interval when her teachers expected her to answer.

In testing for aphasia, the patient at times showed a marked inability to name objects. She would hesitate and finally describe the function of an object; thus a "shoe" was "something to put on your foot," a "hat" was "something to cover your head." The correct name was promptly recognized when given.

Other tests showed no disturbance in distinguishing right from left, no difficulty in sorting or naming colors, no finger agnosia and no other evidence of apraxia. There was left-eye dominance.

The learning ability of the patient again demonstrated the cleavage between the thinking and mechanical abilities. However, it was noticeable that with intensive

training, she would overcome her difficulties to some extent. Her right-handed spelling and recollection of historical dates were more accurate when she received intensive instruction in regard to particular words or facts. However, new words would again precipitate the same errors and it was apparent that, at best, she could only learn to cover up her difficulties by round-about methods.

Psychiatric Background. The psychiatric background of the patient was investigated. It was learned that her early development had been slow. She did not walk until her eighteenth month and did not talk until she was two years of age. Early in infancy she rejected the breast and was a feeding problem for many years. When she began to feed herself, she showed a natural inclination to use the left hand. This tendency was gently but persistently discouraged by the mother, who insisted on transferring the spoon each time to the right hand. When the child was old enough to attend school, she used her left hand in writing but again encountered resistance, this time from a teacher who demanded that she hold her pen in the right hand. She was gradually trained to use her right hand consistently.

In her early childhood, the patient was quiet and obedient. About five years ago, when she was nine years of age, a younger sister was born. It was soon noticed that there was a change in the patient's attitude. She became sulky and quarrelsome and from the first she obviously resented the existence of the younger child. Her discontent became all the greater when her parents suffered financial reverses soon after the birth of the sister and she became deprived of toys and small luxuries to which she was accustomed. She was particularly unhappy because she and her mother no longer accompanied the father on business trips outside New York, experiences which had been very enjoyable. The patient frankly blamed all this on the younger sister, to whom she always referred as "the brat" and with whom she was continually quarreling and fighting.

Since the onset of the present illness, the patient has been under a great emotional strain. She has overheard the conversations of her parents, who have discussed opinions of the various doctors she has visited. She learned that her parents believed she had a degenerative disease of the brain and would probably not survive long. The patient appears to have comprehended the implications quite well. In her distress she ran away from home twice, taking refuge with friends whom she told that she was not wanted at home because her parents cared only for her younger sister. Once in a suicidal attempt she took iodine, which was recovered by an ambulance surgeon who pumped her stomach. It could not be learned whether a similar motive contributed to the trolley "accident." A recent additional source of emotional distress has been the fact that her playmates shunned her because of her twitching and crying spells. Her illness, which requires her to spend a good deal of her time at home in the company of her mother and sister, has heightened the family tension.

Under observation in the hospital, the patient has usually been cheerful, co-operative and interested in her surroundings. However, she has not been inclined to talk about her emotional problems and little was learned about her attitude in this respect.

Summary. A 14 year old girl with degenerative disease of the brain revealed a spelling disability characterized essentially by a tendency to reverse the sequence of letters. These mistakes occurred in oral spelling and in writing produced by the right hand. When the left hand was used in writing, such errors were very rare. The patient realized her mistakes when she was able to visualize them. Related disturbances were found in other spheres, such as recollection of names, addresses and dates.

Aside from these disorders, the patient was of normal intelligence. There was a history of a natural disposition to left-handedness which had been obscured by training in the use of the right hand. Tests also showed dominance of the left eye.

COMMENT

* The spelling difficulty and similar disturbances encountered in this case may conceivably result from organic, functional or psychogenic disorders. However, the specific disability consisting of reversals in the automatic reproduction of visual and auditory symbols, such as is found in left-handed children, indicates that the functional element is of great importance. The special factors which distinguish this case from others of a similar nature (1) are the presence of organic brain disease, the simultaneous ability to write correctly with the left hand while writing incorrectly with the right hand, the close association between memory and handedness, and the onset long after writing and spelling have been learned.

Reversals of letter sequence within words are frequent occurrences in aphasic disturbances. They are related to confusions in the order of syllables and words and probably belong essentially to the entire category of reversals of automatic behavior which are found in functional and organic brain diseases. In this class belong such phenomena as mirror-writing, retropulsion in attempting to walk forward, closing doors instead of opening them, and similar blunders which have been described with organic lesions of the brain. Resembling these are the "undoing mechanisms" of psychogenic origin.

The rôle which disorders of cerebral dominance play in producing these reversals has been demonstrated by the fact that mirror-writing and inversions of spelling which appear in instances of suppressed left-handedness are overcome by restoring the natural use of the hands. The occurrence of spelling disorders in aphasia also confirms the impression that reversals of automatic behavior are associated with disruptions of the functional dominance of one hemisphere.

Although cerebral dominance appears to be determined chiefly by hereditary factors, there is good evidence that such dominance may also be established by training. A possible explanation of the spelling and related disturbances found in this case might postulate that the diffuse degenerative process affecting her brain had resulted in a break-down of the artificial dominance of the left hemisphere with a resulting restitution of natural dominance to the right hemisphere. In the transition state of this break-down, she might be expected to pass through a stage similar to that of left-handed children who are artificially building up a right-sided dominance and whose conflict is reflected in just such tendencies as spelling inversions. This assumption would be in accord with Ribot's law, which

states that in cases of regression, the older and more natural functions are the last to go. The conflict for dominance takes place both on the physiological and psychological levels and it is obvious that emotional influences may be decisive in determining the outcome. This is fully confirmed by observations in such cases.

An interesting precedent for the unilateral psychomotor disturbances manifested in our patient is found in the well-known case of Liepmann (2) which was the starting point for his concept of apraxia. Liepmann's patient suffered a cerebral accident which left him apparently demented. Liepmann was able to show that the senseless behavior of his patient was due largely to a right-handed apraxia whereas the left hand was able to function normally. Strangely enough, the patient was not only unaware of the difference in performance between both hands but showed a preference for the use of the apraxic right hand. Such failure to recognize the disability of the affected side has been frequently observed with organic lesions of the brain.

Following current psychological explanations of such disorders, the specific defect in spelling which our patient presents is probably determined by some fundamental disturbance in spatial perception and in the recognition of the *gestalt* relationship of the part to the whole. Impairment of the functional organization of the brain in dominant and subjugate portions may well be expected to produce such a disturbance.

DISCUSSION

DR. PAUL SCHILDER: This is indeed a very fascinating observation which has been very carefully worked out. As far as I know, there is no other instance in the literature where the spelling by one hand was different from the spelling with the other. One should give such an unusual case a considerable amount of attention. I will start the discussion with the problem of dominance. It is interesting that Dr. Kanzer has quoted the famous case of Liepmann (2) in which there was an apraxia of the right hand. Liepmann thought that this symptom was caused by a lesion of the fiber tracts of the supramarginal gyrus in the left hemisphere. Today we assume that apraxia is not due to a lesion of connecting tracts but to a lesion of a center in the left supramarginal gyrus. In a later communication Liepmann has mentioned that the function of the left hand was impaired, too, although in a minor degree. If the left center does not function correctly, the centers of the right hemisphere show an impairment of function. We are dealing with a "sympathic" apraxia of the left extremities. This is the term used by Liepmann. Sympathic apraxia, later on observed frequently, is based upon the fact that the left hemisphere is also dominant concerning motility. When the dominant left center is destroyed or cannot get its impulses through the corpus callosum to the

right center then the left hand sinks to a lower level of function. The left hand becomes awkward and cannot perform movements in the right way. Nothing is lost; it is merely a function of a lower degree of development. Parts of the left hemisphere are necessary in order to give the full development to the function of the left hand. A similar mechanism is present in this case. This case is obviously one in which the right hemisphere is dominant. Only when the right hemisphere is functioning, and the patient is writing with the left hand, is a good or a comparatively good function in writing and spelling achieved. When, however, the left hemisphere is functioning and the patient is writing with the right hand, then the brain is functioning on a lower level. We deal here with an excellent instance of a problem relative to cerebral dominance. It is of course not an apractic phenomenon in the right hand but a difficulty in spelling with the right hand when the dominant hemisphere is not in full action. I really think this is the unique feature of the case.

What in this case is the function on a lower level, the function which is without the help of the dominant right hemisphere? We have heard about reversals. I would like to make the following general remark. We generally speak about reversals when single letters or the sequence of the letters are reversed; *c* might be changed into *d* and vice versa; *was* into *saw*. It is a change in left-right orientation. This would be called a true reversal. However, we should distinguish reversals of this type from changes in sequence which is a much more general connotation. A change in the sequence of sounds and letters takes place in the speech disturbances in cases of general paralysis. In such cases we have no right to talk of reversals. Such changes also take place in instances of motor aphasia. The patient changes the sequence of letters (sounds) without merely reversing from left to right or vice versa. Dominance does not only consist of the left-right direction being preserved but dominance has generally an influence on the preservation of the correct sequence in speech, in reading, and in writing. One should go one step further in studying dominance. Not only sequences are altered in their correct development by the lesion of the dominant hemisphere but also the whole orientation in space; not only the orientation between left and right but also the orientation between below and above, in front and behind. The correct orientation in space is only possible when the dominant hemisphere is functioning correctly. This comes out in the fact that in form disturbances due to an insufficient function, figures are turned around not only 180° but sometimes 90° . We find also a complete turning upside down. The complete function of the brain takes care that the sequences in speech, writing and spelling are correct also; that forms are orientated in the correct way in space concerning left-right, below-above, in front and behind. We have to reckon in this case also with form disturbances which are not only due to reversals.

However, there are in this case other interesting types of primitive functioning. We find condensations—the word “witch” is condensed with “which.” We meet therefore as primitive signs of speech and spelling functions condensations, reversals, changes in sequence and finally additions of single letters and subtractions of single letters. It is remarkable that all these primitive functions come into appearance in writing only when the dominant right hemisphere is not specifically functioning and the function of the inferior left hemisphere has its sway.

I would like to make one more remark. I think that such disturbances can be due to localized lesions. In this case, however, we have indications of a widespread lesion. There are speech disturbances, form disturbances and disturbances in spelling. An exact localization of the lesion in this case is not possible.

It would be interesting to learn more about the relation between the psychological and organic factors in this case or in cases of this type in general. I think we should distinguish between the different types of psychological reactions in organic brain disease. We must first take into consideration that symptoms due to organic brain disease show in their finer mechanisms physiological and psychological features which correspond to the mechanisms which we find in normal psychological states:—condensations, additions, subtractions and changes in sequence, occurrences which we have learned from dream analysis. Psychological mechanisms found by psychoanalytic methods and the psychological mechanisms which are found on close investigation of organic brain disease are identical. Furthermore, the organic psychological change of every case of this type reverberates into the consciousness. When we deal with a case of reading disability the individual, impaired in his function of reading, in addition does not even want to try to read. The feeling of strain and stress I would call the immediate reflection of the organic disturbance into the consciousness. This immediate reflection of organic disturbance into the consciousness provokes a psychological reaction of a compensatory type. We find, for instance, that these cases develop an enormous interest in mechanical things. This is obviously in relation to the organic lesion. However, it is not of the same order as the unwillingness of the child to try to read. The compensatory reaction is a psychological attitude of different order. Finally, the compensatory reactions of psychological character in the organic cases are immediately related to the general pattern of the personality. The child with reading disability who has been pushed in reading and has not had any outlet concerning compensatory work and mechanical occupation, will become obstinate. It develops an emotional pattern that is in connection with the brain lesion. We find in this case clear evidence of what we have to expect in every case of this kind. The excellent work-up of the case gives a good insight

in the interrelation of these different organic and psychological trends. The case brings in addition a really new observation relative to a spelling disorder.

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OTITIC AND SPHENOIDITIC HYDROCEPHALUS THE VALUE OF THE AYALA INDEX

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That an acute hydrocephalus may accompany a mastoiditis was first commented upon by Taylor (1) in 1890. Symonds (2) in 1931 emphasized the therapeutic importance of differentiating what he called otitic hydrocephalus from another complication of otitic disease, namely, brain abscess. We are reporting a case of hydrocephalus complicating infection of the cranial air sinuses and suggest a practical method of differentiation of hydrocephalus from brain abscess.

It is conceivable that if infection in one group of air sinuses, namely, the mastoids, can produce the syndrome of hydrocephalus, acute inflammations of the other sinuses may also have this complication. Cerebrospinal fluid pressure studies have been made in cases of ocular complications of sphenoidal sinusitis which have indicated the presence of an acute hydrocephalus. Carmack (3) reported one case in which he studied the spinal fluid pressure. There was a history of vague visual disturbances of a month's duration and a somewhat longer history of severe occipital headaches radiating down the spine. Bilateral papilledema was discovered. On lumbar puncture, the pressure of the cerebrospinal fluid was found to be fourteen millimeters of mercury. Apart from this finding there was no abnormality of the spinal fluid. The neurological impression was that there was increased intracranial pressure with no localizing signs. The otolaryngological diagnosis was suppurative ethmoiditis and sphenoiditis. Pus was found bilaterally in the sphenoid and ethmoid sinuses. The day following this operation a lumbar puncture showed clear fluid under a pressure of twenty millimeters of mercury. The patient gradually recovered and two months after operation the eyegrounds had returned to normal and the vision was 20/20 in each eye. Etienne (4) recorded a case of sphenoidal sinusitis with papilledema and an increased spinal pressure of 22 (Claude).

CASE REPORT

History. A sixteen year old high school boy was admitted to The Mount Sinai Hospital with the complaints of occipital headache and pain in the neck for a period of three weeks. The family history contained no significant data. For twelve years the patient had been wearing glasses because of nearsightedness and a squint. Nine

years prior to admission a tonsillectomy was performed and two years before a nasal operation was done (turbinectomy). Head colds were frequent during the six month period before his admission to the hospital.

A submucous resection was performed five weeks before admission. Following this operation he was well for two weeks. One afternoon while at school he began to feel a stiffness and soreness of his neck. In the evening he developed a moderately severe, constricting headache which he localized to the left occipital and post-auricular regions. His temperature was found to be 102°F. This fever continued for four days. He remained in bed for nine days during which time the stiffness of his neck gradually diminished but never entirely disappeared. He noted that the headaches usually appeared in the late afternoon and evening and seemed to be aggravated by excitement or physical or mental exertion. He then returned to school and felt well for three days. The headache returned, without fever or nuchal stiffness but became increasingly constant and severe. On several occasions when he removed his glasses he noticed a transitory blurring of vision in his left eye. During the three weeks before his admission he lost a few pounds and felt weak.

Examination. The patient was a thin sallow youth with cold extremities; he was ambulatory and did not appear acutely ill.

The neurological examination revealed a slight nasal dysarthria. The vision was normal when corrected; there was a mild right internal strabismus but the ocular movements were normal; bilateral papilledema was found with an elevation of three diopters. A slight right mimetic facial weakness was noted. The left ulnar and radial periosteal reflexes were more active than the right. There was some stiffness of the neck. There was slight percussion tenderness in the left suboccipital region.

The mental examination was negative; his behavior was entirely normal.

Tenderness over both antra was present as well as a purulent post-nasal discharge. The lymph nodes at the left angle of the jaw and in the left posterior cervical triangle were enlarged and tender. The blood pressure was 130 systolic and 84 diastolic and the pulse rate was 110 per minute. There was a systolic murmur over the entire precordium which disappeared when the erect posture was assumed. The otoscopic examination was negative.

Laboratory Data. Caloric tests yielded normal responses. Lumbar puncture yielded clear fluid with an initial pressure of 170 mm. of water. The Ayala index was 7.5 and there were five lymphocytes per cu. mm. The spinal fluid chlorides, sugar and total protein were normal in quantity. The white blood count was 18,200 with 80 per cent polymorphonuclear leucocytes. The urine was normal. The blood and spinal fluid serology was entirely negative. A roentgenogram of the paranasal sinuses showed clouding of both antra with thickening of the lining membranes; there was thickening of the lining membrane of the left frontal sinus and the ethmoids on both sides were slightly clouded. Blood culture performed during the period of spiking temperature showed no growth.

Course. During the first few days in the hospital his temperature was subfebrile with no change in his condition. It was the opinion of the observers that there were no localizing signs referable to the central nervous system and that the prime indication was to treat his sinuses. Accordingly, on the fourth hospital day a left sphenoidectomy was performed. The findings were a softened and necrotic anterior wall of the left sphenoid with serous discharge and polypoid tissue in the left ethmoid region. Culture of the discharge from the left sphenoid showed *Streptococcus haemolyticus* (B).

Following this operative procedure the temperature continued only moderately febrile for three days and the patient felt somewhat improved. On the fourth day after the operation the temperature rose to 104°F. and continued intermittently for three days. The sphenoid was examined again with the purpose of removing as much

of its wall as one dared, the preoperative assumption being that an osteomyelitis of that bone was present. At operation an accessory sinus was entered which had a thickened mucous membrane but no changes in the basisphenoid suggesting osteomyelitis were found.

The temperature gradually returned to a normal level. Four days after the operation the patient complained of a hearing defect on the left side. The left ear drum was found bulging. A myringotomy was done. Pus was obtained. The culture showed *Streptococcus haemolyticus* (B), (the same organism had been cultured from the sinuses).

The ear continued to discharge pus; the sphenothmoidal irrigations continued to yield flakes of muco-pus and the temperature remained elevated. Three days after the myringotomy the patient complained of a throbbing ache in the left ear associated with occipital headache. The next day definite mastoid tenderness was noted. The papilledema remained at 3 diopters elevation and the neck was stiff. Fleeting mental symptoms were observed, such as irrelevant spontaneous utterances. Because of the possibility of a brain abscess an encephalogram was performed. This showed a symmetrically dilated ventricular system. There was diffuse clouding of

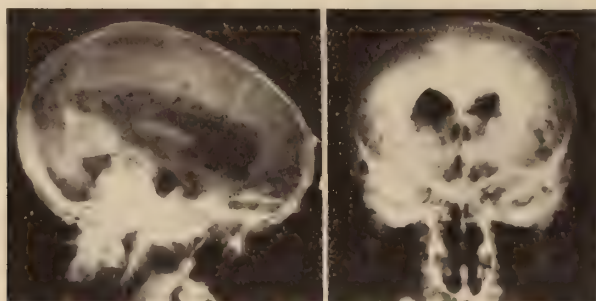


FIG. 1. Views of encephalograms showing hydrocephalus

the mastoid cells on the left. Four days following encephalography a simple mastoidectomy was performed on the left side. An extensive acute mastoiditis was found and the diseased cells were exenterated. On the third postoperative day the temperature returned to normal and, except for an occasional slight rise, remained so during the rest of his hospital stay.

The patient's general condition improved gradually. A number of factors, however, suggested intracranial suppuration; the papilledema remained at 3 to 4 diopters elevation; the patient complained of persistent headache; there was continued nuchal rigidity; the spinal fluid pressure became elevated to 300 mm. of water and for a long period remained above 200 mm.; mental symptoms recurred from time to time. Localizing signs of an abscess were, however, absent and the Ayala index remained persistently high (6 to 7.5).

Another encephalogram was done. This showed a slightly more marked but symmetrical internal hydrocephalus. Later during convalescence still another encephalogram was performed for therapeutic purposes. This last aerogram again showed no deformity of the ventricular or subarachnoid spaces.

The mastoid wound healed, the nasal discharge disappeared and gradually the nuchal pain on flexion subsided. Roentgenograms of the cervical spine had been repeatedly negative. At the time of his discharge the papilledema was showing signs of regression and the spinal fluid pressure had fallen to 190 mm. of water. Meningeal permeability was determined by using the method of Walter. The quo-

tient of 3.3. was within normal limits. Perimetric studies were normal except that shortly before discharge from the hospital there was a slight constriction of the color fields. Visual acuity had remained normal throughout.

One month after discharge a follow-up note revealed significant subjective improvement. Papilledema was still present.

COMMENT

From the picture presented on admission there was clear indication for operative treatment of the sphenoid and ethmoid sinuses. Papilledema and cerebrospinal hypertension were present before the mastoiditis became manifest. Still, the infection may well have been smoldering in the mastoid for the entire period of morbidity so that the hydrocephalus cannot be considered as wholly sphenoiditic in origin. With the persistence of headache, papilledema and increased spinal fluid pressure, the differential diagnosis clearly rested between brain abscess and an acute hydrocephalus. The absence of localizing signs did not militate against a diagnosis of brain abscess. The Ayala index was originally 7.5 and on all subsequent lumbar punctures remained above 6.0. In a series of eleven verified cases we found only one instance of brain abscess with an Ayala index above 5.0. The exception was a ruptured abscess with bacterial meningitis. One of these brain abscesses, (reported by Kaplan (5)) was secondary to a sphenoidal sinus infection. In this patient there was an elevated cerebrospinal fluid pressure and an Ayala index of 3.8. The diagnosis of brain abscess was at first not clearly defined as localizing signs were sparse. Ultimately the diagnosis of brain abscess was verified by operation. In the case reported in this communication, substantiation of the diagnosis of hydrocephalus was made by three encephalographies (Fig. 1). The progressive improvement of the patient corroborated our hypothesis. The Ayala index has been used in the differential diagnosis of otitic hydrocephalus (6). Wherever the index was above six we suggested treatment of the otogenous focus. We felt fairly positive in all these cases that there was no suppurative intracranial complication.

The Ayala index (7) is computed in the following way:

$$\frac{\text{final pressure}}{\text{initial pressure}} \times \text{amount of fluid removed (10 cc.)}$$

The case presented is of additional interest because it is one of the few reported in which encephalographic studies have been performed. That a definite communicating hydrocephalus is present cannot be doubted after examination of the X-ray films. Whether the hydrocephalus is due to increased production of cerebrospinal fluid or to a decreased absorption, cannot be stated.

It is important for the otolaryngologist to bear in mind the possibility of a hydrocephalus complicating sphenoiditis as well as mastoiditis. Whenever papilledema and elevated cerebrospinal fluid pressure are

encountered, the Ayala index can serve as a valuable guide in the management of the case.

CONCLUSION

A case of hydrocephalus complicating cranial air sinus infection is reported. The value of the Ayala index in differentiating this condition from brain abscess is emphasized.

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SUBCORTICAL DEGENERATIVE ENCEPHALOPATHY (SCHILDER'S DISEASE)

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The authors of this paper have had the opportunity to study in detail a case of diffuse sclerosis, or Schilder's disease. A fairly comprehensive survey of the literature revealed that not many more than one hundred verified cases have been described. Despite the comparative rarity of the disease, a mass of literature has accumulated, much of which deals with the controversial nature of the underlying pathological process. The lesions were considered by some observers to be inflammatory and by others as degenerative in etiology. This controversy has centered, for the most part, about the problem of the essentially inflammatory or degenerative nature of the lesions. The case herein presented, reveals clear-cut pathological findings, which may throw some light on this problem.

CASE REPORT

History. F. S., aged 6 years, was admitted to Newark Beth Israel Hospital on December 31, 1934. The patient was one of five children, ranging in age from six to fourteen years. She was one of a pair of binovular twins. The other children were all alive and healthy.

The child had been apparently well until the latter part of January, 1934, when, while at play, she fell down a flight of thirty-two steps. She was momentarily stunned and suffered a slight nosebleed, but recovered within a few minutes and returned to play.

One week after the accident, the mother noticed that the child walked in a staggering manner and that, when seated, she swayed unsteadily from side to side, occasionally slipping from her chair to the floor. She gradually became weak, unable to hold either a fork or spoon for more than a few minutes, dropped objects from her hands and experienced increasing difficulty in dressing herself. She had several nosebleeds which ceased after five days. The child became listless, talked less frequently, did not appear eager to play, and suffered considerable loss of weight and appetite. She did not complain of pain, but frequently stated that her head felt "funny". The child became more quiet and had difficulty in remembering the names of her brothers and sisters.

Her condition became progressively worse. She was unable to recognize her mother. Her speech became unintelligible and her actions became so violent that, at times, physical restraint was necessary.

After a period of nine months in another hospital, she was removed against advice. At the time of her removal, the child was unable to talk or move about and recognized no one. She would lay for hours looking at the ceiling, had to be fed, and had lost all coordination of movement. The hands were held tightly clenched, the legs were very stiff. There were constant twitching movements of the extremities. The skin was tightly stretched over the bones of the entire body. Despite the rigidity of the jaw and difficulty in eating, the appetite was excellent. Hearing gradually diminished so that she appeared to be totally deaf. If moved quickly or abruptly, she appeared to be in pain.

In January, 1935, one year after the onset of symptoms, the child was admitted to the Beth Israel Hospital because of an acute respiratory infection.

The child was emaciated, lay in bed staring about the room or at the ceiling for long periods of time, practically motionless except for involuntary movements of the extremities. Although the child made varied sounds on stimulation, no speech could be elicited. She was apparently unable to see and did not react to sound. The optic discs were pale and suggestive of an optic atrophy. The cranial nerves were otherwise negative. Marked rigidity was present throughout the body. The reflexes were present throughout, but were markedly inhibited by the degree of rigidity present. The Babinski sign and confirmatories were obtained on both sides. Numerous movements of choreiform and athetoid types were noted. Signs of bronchopneumonia were found.

Laboratory Data. The cerebrospinal fluid contained one cell per cu. mm. The globulin reaction was normal. The Wassermann and colloidal gold tests were negative.

Course. The examiner (L. H. L.) felt that the diffuse and bilateral nature of the findings indicated a widespread involvement of the central nervous system and a diagnosis was made of *subcortical degenerative encephalopathy*.

The child ran a moderate temperature. Her general condition rendered further investigation impossible. Death took place on January 3, 1935, four days after admission.

NECROPSY FINDINGS

Gross Anatomy. Except for evidence of bronchopneumonia, the abnormal findings were restricted entirely to the cranial cavity. The leptomeninges appeared to be normal. The convolutions and sulci presented no alterations.

The brain felt rubbery and fibrotic to the touch. On sectioning the brain, the gray matter appeared normal. The white matter felt firmer than usual in consistency. No localized lesions were noted and no evidence of an old trauma was found. Coronal sections of the brain were made after fixation in 10 per cent formalin. The ventricles were of normal size. The gray cortex was of normal thickness and no gross lesions were seen in the subcortex. No patches of softening or discoloration were found. Sections through various levels of the brain stem revealed no gross abnormalities.

Microscopic Anatomy. Sections, taken from various parts of the brain, were stained with hematoxylin and eosin; Nissl, Spielmeier, Weil and Pal-Weigert stains for myelin; Herxheimer's scarlet red and the Marchi method for fat; the Cajal gold sublimate, the Hortega silver carbonate; the Holzer methods for glia and glia fibers; and the Bielschowsky method for axis cylinders.

Gray Matter. The cortex was everywhere well preserved; the lamellations presented their normal appearance in all the cerebral lobes. Slight pathological changes were noted in a few nerve cells, particularly in those of the frontal lobes. Here and there, an occasional pyknotic, shrunken nerve cell was encountered and a few nerve cells showed a loss of Nissl substance. The Betz cells were intact. Occasionally

a dense accumulation of glia cells about a disintegrating nerve cell was encountered (Fig. 1). Fat was present only in very small quantities and practically always collected in cells along the blood vessels in the deepest cortical layers. More marked changes were found in the glia. There was a fairly marked increase of the microglia and macroglia in the deepest layers of the cortex. (The astrocytes were of normal size, with numerous long, fibrillary processes, and showed a characteristic tendency to accumulate along blood vessels.) The microglia were increased in number; many of them possessed thickened bodies with short, thick processes. No swellings, vacuolization, or transformation into compound granular corpuscles was noted. The myelin sheaths and axis cylinders in the cortex presented no abnormalities. Except for slight infiltration in places with fibroblasts and mononuclear cells, the meninges over the cortex were normal.

White Matter. In the Nissl preparations, the white matter of both hemispheres appeared in a much lighter tint than usual, while, in the hematoxylin and eosin stained sections, it stained in an uneven and irregular manner. This was especially

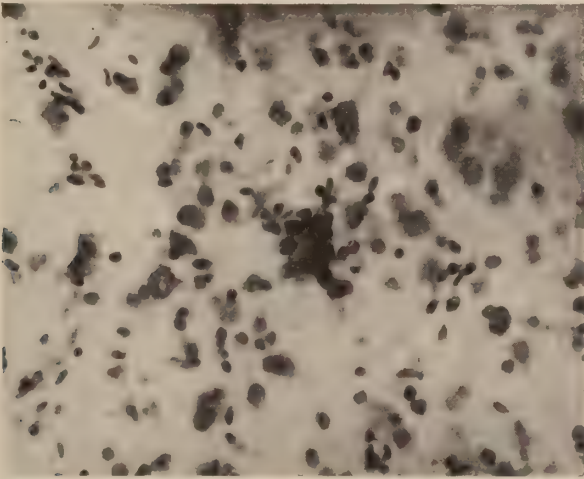


FIG. 1. Nissl stain. Frontal cortex. Accumulation of glia cells. ($\times 460$).

marked in the deeper parts of the white matter, where the tissue appeared full of minute holes and irregularities. In these areas the small blood vessels appeared to be more numerous. This impression was caused by the *rarefaction* of the parenchyma. Accumulations of oligodendroglia and gitter cells were noted along many of the vessels. An occasional plasma cell was also present. These perivascular accumulations were usually quite mild, never forming conspicuous perivascular cuffs. The cells never infiltrated the vessels themselves, but were collected in the Virchow-Robin spaces, or more loosely in the surrounding parenchyma. No foci of perivascular lymphocytic infiltration were found.

The cellular elements in the white matter were greatly increased, especially in the more rarefied areas described above. The types and character of these cells will be described later in the discussion of glial changes.

Fat Preparations. In the Herxheimer's scarlet red and the Marchi stains, a diffuse and widespread deposition of lipoid was noted in the white matter of both hemispheres. These deposits were strikingly restricted to the white matter, which was sharply demarcated from the gray matter by the stained masses of fat (Fig. 2).

These fat deposits consisted of round, oval and irregularly shaped globules, varying in size from minute droplets to large masses. Throughout the white matter, there was a similar distribution of the fat. This consisted of a gradual increase in the quantity, as well as in the size, of the globules, as one proceeded from the subcortical zone into the deeper portions of the white matter. It was in the areas which cor-

FIG. 2



FIG. 3

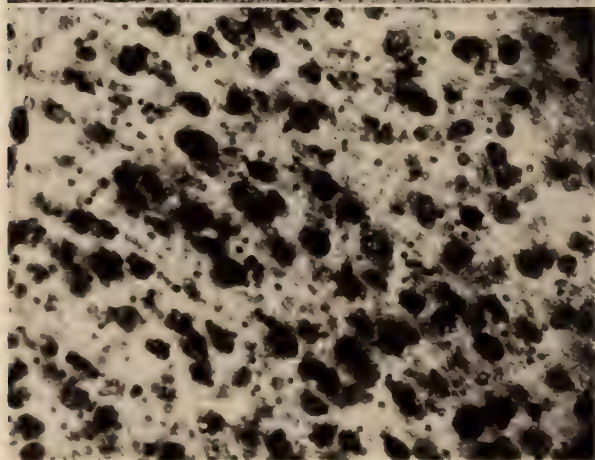


FIG. 2. Scarlet red stain. Fat deposits restricted to the white matter. Accumulation of fat about a blood vessel.

FIG. 3. Scarlet red stain. Large masses of fat in the deeper portion of the white matter. ($\times 400$).

responded to the most rarefied regions in the Nissl and hematoxylin and eosin stained sections, that the dense collections of large fat masses were found (Fig. 3). Although closely packed, these masses frequently assumed a poorly defined linear distribution, evidently along degenerating myelin sheaths. The fat globules were contained, for the most part, in compound granular (gitter cells) corpuscles and also to a lesser degree in the swollen astrocytes. Considerable fat, however especially smaller

globules, lay free in the tissues. The fat-containing gitter cells frequently accumulated in the perivascular spaces (Fig. 2), particularly in the more superficial subcortical zones. Immediately beneath the gray matter, in the regions of the U-fibers, a rim of white matter free of fat deposits was frequently noted. No significant difference in the quantity of fat could be detected in the various lobes of the brain. The heaviest deposits were found consistently in the deepest part of the white matter, that is, in the centrum semiovale, while a gradual quantitative decrease toward the periphery of the white matter was noted.

Myelin Sheath Preparations. Sections stained by the Spielmeyer, Weil and Pal-Weigert methods showed a diffuse and extensive demyelination which involved the entire cerebrum. On gross inspection of the sections, the white matter did not present the normal deeply stained appearance of such preparations, but appeared much more lightly stained. Although this defective staining also involved the superficial layers, it was most marked in the deeper portions of the subcortical white matter. In many places, a thin, deeply stained line, immediately subjacent to the

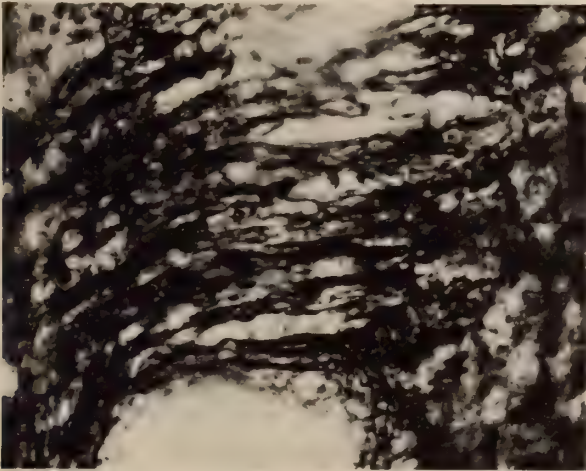


FIG. 4. Weil stain. Precentral gyrus. Degenerating myelin sheaths. ($\times 460$).

gray matter, in the region of the U-fibers, sharply separated the gray cortex from the poorly stained white matter. On microscopic examination a marked reduction in the quantity of myelin sheaths was seen. This reduction which became more marked as one proceeded from the superficial to the deeper portions of the white matter was diffuse so that, except for a few very small foci, no areas of complete demyelination were found. The degenerative changes were especially noted in the rarefied portions of the deep white matter. The individual sheaths, many of which were undergoing degenerative changes were arranged in parallel rows and stood out conspicuously. The sheaths were thickened and irregularly swollen, and possessed the ballooning and bulbous swellings characteristically seen in degenerative processes of the myelin (Fig. 4). Small round globules of myelin were scattered along these sheaths, but no large myelin balls were found. The destruction of myelin involved the frontal more than the other lobes. No foci of demyelination were found in relation to the blood vessels.

Axis Cylinders. Changes in the axis cylinders were present, corresponding in distribution and severity to those noted in the myelin sheaths. Throughout the en-

ture white matter, thickened, fragmented and broken cylinders were found. Corresponding to the areas of maximum myelin loss and fat deposition, the most profound loss and destruction of axis cylinders was observed in the deepest portions of the white matter. From the changes in the white matter, it was impossible to conclude whether the pathologic process was primarily a myelolytic or a neurolytic one. The degree to which these two structures were injured by the pathologic process appeared

FIG. 5

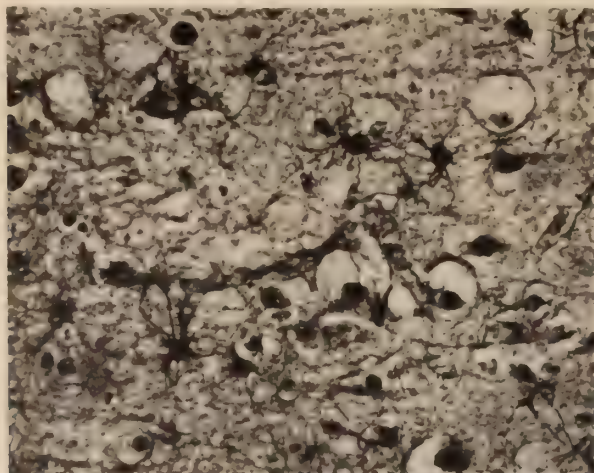


FIG. 6

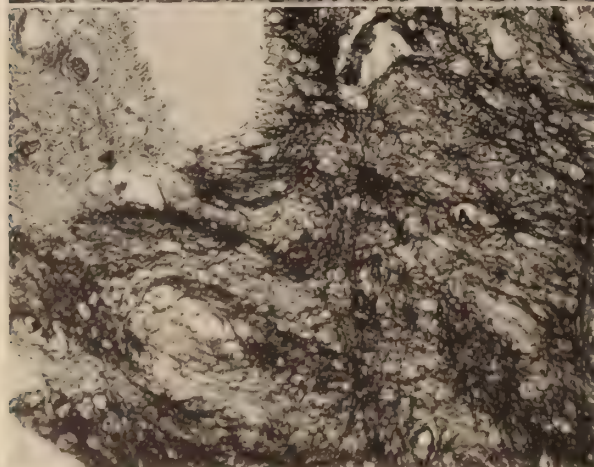


FIG. 5. Cajal gold sublimate stain (Globus modification). White matter, frontal lobe. Astrocytosis; many large and pathological astrocytes. ($\times 150$).

FIG. 6. Holzer preparation. Glia fibrosis in deep white matter. ($\times 220$).

to be about equal. In the few minute foci of complete demyelination, the axis cylinders were not preserved. The nerve fibers in the gray matter, however, being well preserved and showing no degenerative changes, suggested that the noxious agent attacked the white matter, that is, the myelin, first, and that the destruction of axis cylinders then proceeded hand in hand with the demyelination.

Neuroglia. The neuroglia was severely affected by the pathologic process and

showed both progressive and regressive changes, involving all three types of glia. The most marked alterations were in the macroglia and the microglia, while the only change noted in the oligodendroglia was a quantitative increase. The astrocytes in the region of the U-fibers and in the deepest cortical layers were numerically increased and distributed along blood vessels, but showed no regressive changes. In the subcortical white matter, however, and particularly in the deeper portions where the demyelination was most severe, pathological macroglia were noted in increasing numbers. When stained with hematoxylin and eosin and with the Nissl stain, many astrocytes were seen to be of the gemästete type, with large, plump, pale-staining bodies, and pale-staining nuclei, eccentrically situated. Short, thick processes were frequently visible, even in these preparations.

In the Cajal gold-sublimate preparations, diffuse astrocytic proliferation throughout the white matter was well demonstrated (Fig. 5). Large hypertrophic forms, frequently with rounded bodies and short, thick processes (ameboid glia) were present. As one proceeded from the subcortical to the central portions of the white matter, a progressive increase in glia fibers was noted. In these regions, the Holzer stains revealed dense, interlacing masses of robust glia fibers, in which were numerous, large, fiber-forming astrocytes (Fig. 6).

The alterations in the microglia consisted of both quantitative and qualitative changes. This was especially conspicuous in the deeper parts of the white matter and in the same areas where the most massive fat deposits were found. As one approached these areas, many microglia cells became thickened and rounded, the bodies assuming various bizarre shapes, while their processes became shortened, thickened and deformed by irregular swellings and vacuoles. As the bodies became shorter and rounder, the cytoplasm began to assume a skeinlike and vacuolated appearance, until they finally appeared as large, rounded, vacuolated cells with small, dark, peripherally situated nuclei. At this stage, some of these cells still possessed short, thick processes. When these processes were finally lost, typical gitter cells emerged as the final stage of this metamorphosis. In the cortex, at its junction with the white matter, some hypertrophy of the microglia cells was found also, but no gitter cells or changes like those described above.

The glia alterations, although diffuse and widespread in the white matter of both hemispheres, were most pronounced in the frontal lobes.

Basal Ganglia. Sections through the corpora striata and thalami revealed normal nuclei, but in the internal capsules there were diffuse, fairly extensive, deposits of small lipoid globules, lying free in the tissues. The amount of fat was much less than that present in the white matter of the cerebral hemispheres. Small amounts of fat were also found in a few vessels in the gray matter, the corpora striata and thalami. The myelin sheaths, however, showed no degenerative changes and no demyelination was found. The axis cylinders were unaffected.

The optic tracts were free of pathologic changes.

The midbrain, pons, and medulla showed the same type of alteration. Although they showed no loss of myelin or degenerative changes, the pyramidal tracts contained fat throughout their course, but in decreasing amounts as one proceeded caudally. Granular deposits of fat, appearing like black stippling in the Marchi preparations, were present in practically all of the myelinated structures throughout the brain stem, including the cerebellar peduncles. Heavier deposits of fat were found in the oculomotor fibers in the midbrain, and in many of the cranial nerve roots. In the myelin stains, however, no myelin degeneration was noted, and the axis cylinders were intact. Throughout the brain stem, the nuclei and nerve cells were normal, but small amounts of fat were present in the substantia nigra and in the colliculi. The glial elements in the brain stem were normal. No proliferation of glia or formation of gitter cells was found.

The cerebellum showed slight changes consisting of a diffuse black stippling in the Marchi preparations in the deeper white matter, and, to a lesser extent, in the white matter of some of the folia. The myelin sheaths, axis cylinders, nuclei and cortex appeared normal.

COMMENT ON PATHOLOGICAL FINDINGS

Although, according to Bouman, Schilder's disease varies much in both its clinical and pathological features, the anatomical alterations are sufficiently characteristic to permit a pathological diagnosis in most cases. The case herein described illustrates the typical limitation of the disease process to the white matter, the diffuse but irregular demyelination with relative sparing of the U-fibers, the destruction of axis cylinders in the demyelinated areas, and the progressive and regressive neuroglial changes. That the pathologic process was still in its relatively early form is suggested by the absence of complete demyelination, and by the presence of many neuroglia in both the progressive and the earlier regressive stages. This is especially true of the microglia, which are found in all stages of their transition to gitter cells. The macroglial proliferation, which includes many globoid (gemästete) and ameboid forms, resembles closely the type of astrocytic reaction commonly described in Schilder's disease, as does the increase in glia fibers and formation of glia scars.

A finding of considerable importance is the absence of any mesodermal reaction in the form of perivascular lymphocytic infiltration. The sparse perivascular accumulations of cells in this case consist of glia elements, chiefly fat-containing compound granular corpuscles. Although perivascular round cell infiltration is described in the majority of cases, the absence or paucity of a mesodermal reaction in some instances was emphasized as far back as 1916 by Krabbe (2), and in more recent years by Ferraro (3) in 1927, and by Globus and Strauss (4) in 1928. In his monograph, Bouman states that the lymphocytic infiltrations may be mild or severe and cites a number of cases from the literature in which they were absent.

There is a difference of opinion among the various writers on Schilder's disease, as to whether the essential pathological process is inflammatory or degenerative. The reader is referred to Bouman's monograph for a detailed presentation of these views as expressed in the literature. In the attempt to distinguish between these two types of pathological process, great significance has usually been placed upon the presence or absence of perivascular lymphocytic and plasma cell infiltrations. A number of cases have been described in which the complete absence, or relative paucity, of these mesodermal infiltrations, suggested to the authors and, in many instances, to subsequent observers that the pathologic process was primarily one of degeneration. On the other hand, there are many

reports in which severe inflammatory foci are described, on the basis of which the authors considered that the pathologic process was an inflammatory one. Many workers, however, have considered the infiltrative mesodermal alterations a reaction to the tissue destruction, in the sense of the symptomatic inflammation of Spielmeyer, and not as evidence of an infectious process. Krabbe, in 1916, Ferraro in 1927, and Globus and Strauss in 1928, in particular, emphasized the degenerative character of the process, and the latter suggested the name "degenerative encephalopathy" in contrast to Schilder's "encephalitis periaxialis diffusa," which intimates an inflammatory process.

Bouman came to the conclusion that "we cannot yet decide as to the problem of inflammation or degeneration." That considerable confusion exists among the various writers is indicated by Bouman's remark that different authors frequently assign the same case to different categories. Bouman felt that there were cases which were "certainly inflammatory processes," but "also degenerative forms," while "in other cases it was not possible to give a decisive opinion."

In the light of these divergent points of view, the present case is of considerable interest because of the complete absence of any infiltrative mesodermal reaction. Is it possible that inflammatory foci were present during life, earlier in the disease? This is unlikely, for the course was relatively short and progressive, and there is no reason to assume that the histological manifestations of inflammation would have disappeared so quickly. The pathological process has affected only the ectodermal structures in the brain, producing a breakdown of a specific part of the essential neural tissue, accompanied by a proliferative and regressive change in the neuroglia. This type of alteration in the nervous system is usually classified as a degenerative one, in order to distinguish it from inflammatory conditions in which the mesodermal elements play a conspicuous rôle.

This designation, unfortunately, is merely descriptive, and sheds no light on the cause of the destruction of neural tissue. The head trauma was most probably of no etiological significance. Cerebral trauma is cited by Bouman in the list of possible causes, but there is no convincing proof that such trauma plays any rôle in its etiology. Numerous infectious diseases are mentioned as immediately preceding the onset of the clinical symptoms, and are considered by some authors to be of etiological significance, and to support the conception of the inflammatory nature of the disease. In the case under discussion, there is no history of a preceding infection. In these cases, Gasul (5) considers the disease a degenerative one "not as a result of circulating toxins, as Krabbe postulated, nor of a heredodegenerative nature, as in Friedreich's disease, but as a result of vascular disturbances of the white matter."

CLINICAL ASPECTS OF DIFFUSE SCLEROSIS

Etiology. Very little can be said as to the etiology of this disease. Although numerous agents have been cited as important, no one factor is constantly found. Cerebral trauma, influenza, the infections of childhood and pregnancy have been advanced as possible causes.

The hereditary factor is cited by a number of observers and must be given consideration. A number of writers have described several cases occurring in one family, and cases in which other anomalies of the central nervous system have occurred in the same family group containing a case of diffuse sclerosis. No hereditary factors have been found in the family history of this child. It should again be noted that this child was one of dissimilar twins: the twin brother at the time of this writing, two years later, is healthy and shows no evidence of disease.

In the case under consideration, no possible etiological factor, other than trauma, could be discovered. Huebner (6) cited a case in which the onset of symptoms followed a head injury. He also quotes a case of Bullard (7) in which there had been a head injury prior to the development of symptoms. Other writers have intimated a possible connection between trauma and the clinical pictures presented in their cases. The trauma in this case was said to have been mild in character. There was no period of unconsciousness, and within a few minutes the child had returned to her normal activity. No symptoms were noted until one week after this trauma. It is improbable that a blow to the head which did not cause loss of consciousness, would be able to produce the profound changes ultimately found in the brain. One is disposed, therefore, to believe that the trauma was incidental, and of no etiological significance.

So far as can be determined, this child did not suffer from any infectious disease which might be correlated with the clinical manifestations.

Analysis of Clinical Findings. The findings in this case are quite typical of those cases in children reported in the literature. Headache, ataxia and gradually increasing psychic disorders, ultimately lead to a state of complete incoordination and amentia. Bouman states: "In time, the child deteriorates, with regard to his intellect and general behavior." Our case is no exception to this statement. Disturbances of speech are cited by many observers, and were present in our case. As stated in the clinical history, the speech of this patient gradually became unintelligible, and in the end consisted of emitting sounds of a bizarre nature.

At the time the case came under our observation, there were present numerous contractures. These contractures frequently gave way to athetoid and choreiform movements, involving all four extremities. At times, a posture resembling decerebrate rigidity was seen. A fairly marked degree of optic atrophy was noted in our case. Optic atrophy has

been found in a number of cases, as have other abnormalities of the optic nerve. Optic neuritis has been frequently reported; choked discs, mentioned less often. The degree of mental deterioration in our case prevented any attempt to estimate hearing or vision, but no evidence of response to visual or auditory stimuli could be noted.

Bouman's description of the last stages of the illness should be noted: "The similarity in the last stage of the illness in various cases, is remarkable. The face has a grinning expression, the eyes wide open. There are contractures at the elbow joints and wrists. The hands are rolled around; also adducted. The legs are stiff in extension, the feet are turned downward and inward. Psychically, the patient is deteriorating, going on to a terminal dementia, combined with severe cachexia. As a rule, death follows an intercurrent illness." The description in all respects is typical of our case. Death in this instance was caused by bronchopneumonia.

The differential diagnosis of diffuse sclerosis or Schilder's disease, presents great difficulties. We must recognize it as a rapidly progressive malady, usually occurring in children and young adults. The onset is insidious and the course usually progressive, although remissions may occur. The average duration is from a few months to three years. Cerebral blindness is an early sign; ataxia and spastic changes in the extremities are also seen early in the course of the disease. Psychic changes and mental symptoms appear early. The amentia increases and usually leads to a state of coma, together with intense contractures, choreiform and athetoid movements. Elevations in temperature may occur, but are not constant. Changes in the optic nerve are not unusual, as cited above.

SUMMARY

A case of subcortical degenerative encephalopathy (Schilder's disease) is presented, with pathological study. A child of five, one of dissimilar twins, following a very slight trauma to the head, is observed to deteriorate mentally and physically over a period of one year. A state of amentia finally results and death is caused by bronchopneumonia. The pathological manifestations, consisting briefly of diffuse subcortical demyelination and destruction of axis cylinders, with reactive alterations in the macroglial and microglial elements, present the characteristic picture of Schilder's disease. The striking absence of any mesodermal changes of an inflammatory nature is considered a significant finding in support of the concept that the disease process is essentially degenerative.

(We are indebted to Doctor L. Charles Rosenberg, on whose service at the Newark Beth Israel Hospital this case was seen. We likewise are indebted to Doctor Joseph H. Globus for his invaluable aid in the preparation and study of the pathological material. The neuro-pathological work on this case was done under the supervision of Dr. Globus in the laboratories of The Mount Sinai Hospital, New York City.)

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BRAIN STEM SYNDROMES

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Certain syndromes of the brain stem offer little diagnostic difficulty to the experienced neurologist. The clinical picture produced by an occlusion of the posterior inferior cerebellar artery, for example, is so clear-cut that the diagnosis is quite apparent. The same holds true for thrombosis of the superior cerebellar or of the anterior spinal artery. There are other conditions, however, which may baffle the most skilled observer. The reasons for this are, at least, two in number. In the first place, in those cases where the localization of the lesion can be fairly safely assigned to the brain stem, there may be considerable doubt as to the nature of the lesion—whether vascular, neoplastic, inflammatory, or degenerative. In the second place, one is not infrequently troubled by the question whether a single, discrete lesion in the brain stem is responsible for all the neurologic signs observed, or whether disseminated lesions are present in various parts of the neuraxis. Evidence of damage to the nuclear structures in the brain stem or of the nerves originating from them, manifesting itself in a paralysis of the vocal cord or of the soft palate, in weakness of the facial musculature of the lower motor neuron type, or in some form of ocular palsy is usually unequivocal. Involvement of these structures, however, establishes merely the fact that there is a lesion in the brain stem; it does not help to decide whether all the neurologic signs observed, in addition, are due to involvement of other nervous structures at the same level. If one conceives of the brain stem as a bottle-neck, so to speak, for numerous pathways ascending to and descending from the brain, one can readily realize how a lesion of the brain stem may simulate disseminated disease, or vice versa. Vagaries in the clinical course of a disease, resulting, for example, in a neoplastic process taking on the fulminating properties of an acute inflammatory disease, may be cited as an additional source of diagnostic difficulty and error. A small group of representative cases of syndromes of the brain stem is presented to exemplify some of these problems.

CASE REPORTS

Case 1 (Adm. 406395). A girl, aged 8, was admitted to The Mount Sinai Hospital on March 29, 1937. The mother had had a premature labor and four miscarriages prior to the birth of this child. The patient had chickenpox four years ago, scarlet fever two and a half years ago, and measles one and a half years ago. She

was perfectly well until three weeks before admission when she suddenly developed frontal headache, and dizziness. The following day, at school, her handwriting was found to be faulty. Five days after the onset diplopia appeared. Two days later her right extremities became weak and limp. For a few days following this, her condition appeared somewhat better. During the three days preceding admission progression again occurred with increasing weakness of the right limbs, deviation of the eyes, and dysarthria. At times there were incontinence of urine, dysuria, or difficulty in initiating the stream.

Examination. There were ataxia of the left upper limb, right flaccid hemiplegia, with pyramidal tract signs; a right hemisensory syndrome for all modalities over the right side of the body and face; there was evidence of right third nerve and of left third and sixth nerve involvement; the right side of the palate lagged, and the voice was thick and nasal. The fundi were negative. Cerebrospinal fluid was under a pressure of 160 mm. of water and contained four cells. Serology was negative. The Ayala index was 7.5.

A definite diagnosis could not be established at this time. Although a non-suppurative inflammatory process was held most likely, a tumor of the brain stem, perhaps a pinealoma, was considered as a diagnostic possibility, and radiotherapy was instituted.

Course. The patient developed a left peripheral facial palsy. The dysarthria became more marked. Gradually pyramidal tract signs on the left side appeared. About six weeks after admission slight blurring of the nasal margins of the optic discs, which subsequently developed into definite papilledema, was observed. At this time the diagnosis of a pontine tumor was made. The child died seven weeks after admission.

Post mortem examination disclosed a neoplasm of the brain stem, involving mid-brain, pons, and medulla.

Comment. At the outset the diagnosis in this case had to remain in abeyance. The sudden onset of neurologic symptoms and signs in a young individual suggested most strongly an encephalitic process, but at the same time, the possibility of a single lesion, of neoplastic nature, in the brain stem was entertained. The relentless progression of the disease while the patient was under observation and the appearance of papilledema helped to establish the correct diagnosis. The history of transitory improvement, obtained from the patient, is noteworthy, since it is now well established that remissions may occur in the course of a tumor growth, and should by no means mislead one into excluding a neoplasm from the diagnostic considerations.

The following case is considerably more involved, although here, too, the proper diagnosis was eventually established on clinical grounds.

Case 2 (Adm. 386526). A girl, aged four, was admitted to The Mount Sinai Hospital on November 8, 1935. The past and family histories were negative. The child had been well up to eight weeks before admission. At that time the following incident occurred. Her mother had placed her in a baby carriage so that she might sleep out-of-doors. In some way or other—the details were not clear in the mother's mind—she was tipped out of the carriage while asleep, and fell, striking the right side of her head. She became pale and unconscious, and had a generalized convulsion. During the next few days she appeared irritable and fretful. One week after the accident, the mother noted that the right side of the child's face was paralyzed,

there was drooping of the left eyelid, and she could not turn the right eyeball fully outwards. Three weeks after the accident it was noted that the child tended to fall and did not use the left limbs as well as the right. She vomited and complained of headache. During the next five weeks, the child lay in bed, gradually becoming stuporous and apathetic. Constipation was marked. She lost weight, although she consumed food and water avidly.

Examination. The child cooperated poorly. There was a left hemiparesis with pyramidal tract signs; a right peripheral type of facial paralysis was present; the right eyeball was impaired in its movements in every direction except downwards; the right pupil was larger than the left; the right palpebral fissure was greater than the left, and the right eyeball more prominent; there was ptosis of the left lid, more marked when the patient was recumbent. Cerebrospinal fluid was negative in all respects. An X-ray examination of the skull proved negative.

At this time the diagnosis favored was that of post-traumatic hemorrhages into the brain stem. One observer mentioned the possibility of an infiltrating neoplasm of the pons.

Course. Under observation the child became more and more torpid. Spontaneous speech was absent and responses to questions were feeble and fragmentary. She was incontinent of urine and feces. About a month after admission awkwardness and an intention tremor were noted in the right upper limb, in addition to pre-existing signs. Vomiting became a prominent symptom. A few days later several small hemorrhages appeared in the right fundus, and papilledema was noted in that eye. Lumbar puncture showed a pressure of 160 mm. of water. An expanding lesion was then suspected. An X-ray examination of the chest, taken in view of the possibility of a tuberculous process, was negative. The child died about eight weeks after admission to the hospital.

Post mortem examination disclosed an extensive spongioblastoma that had invaded practically all of the brain stem.

Comment. The onset of neurologic disease in a heretofore completely normal child, directly after a severe trauma to the head, made the diagnosis of traumatic hemorrhages into the substance of the brain stem appear the only logical one. Indeed, it is difficult to see how, even after the benefit of this experience, one could avoid a similar error in the future. The short period of relative well-being following the accident would not be decisive, since delayed hemorrhage is known to occur after cerebral trauma. Here, again, only the progressive course, combined with evidence of increased intracranial pressure, led the way finally to the diagnosis of an expanding lesion. With all the available facts, one aspect of the case remains somewhat perplexing. It is inconceivable that a tumor as extensive as this one, growing from the medulla through to the midbrain, should have achieved its size following the head injury. Apparently the tumor was of considerable proportion prior to that time. Yet there were no clinical signs to indicate its presence, until, apparently, trauma activated further growth.

The following case was likewise complicated, not merely by the history of antecedent trauma, but also by a history of chronic alcoholism.

Case 3 (Adm. 328907). A laborer, aged 49, was admitted to The Mount Sinai Hospital on August 8, 1931. He drank about three quarts of wine daily, with an

occasional whiskey, for a great number of years. His second wife, with whom he was now living, had had two miscarriages after the birth of their second child. The patient was well until six weeks before admission. At that time, while he was working in the street, an auto passed, brushing against his hand. He was pushed backwards against some object, striking his head. He did not lose consciousness, and required merely first aid treatment for his thumb. That same night he complained of dizziness, diplopia, and headache. He tended to fall in various directions, especially to the left. The next day his right eyelid began to droop. He became drowsy. He was unable to return to work because of the headache and the instability in walking. During the five days before admission he had difficulty in starting the urinary stream.

Examination. There was evidence of involvement of the right third nerve with mild pyramidal tract signs and cerebellar signs on the left side of the body. Mentally, the patient appeared normal. The retinal arteries were narrow; otherwise the fundi were negative. A few days later, the ocular signs had progressed, so that there was now a third nerve paralysis on the right, and a third and sixth nerve paralysis on the left side. There was considerable tenderness elicited by pressure over the calf muscles.

It was held at this time that if lues was ruled out the most likely diagnosis was a neurologic syndrome on an alcoholic basis: a polioencephalitis superior hemorrhagica of Wernicke. It was evident that the lesion was in the region of the midbrain, yielding a combination of a Weber and a Benedict syndrome. Trauma was considered, at most, to be an incidental or contributory factor.

The serology was negative in the blood. The cerebrospinal fluid was negative in all respects, as was an X-ray examination of the skull.

Course. The patient became restless and drowsy. He showed impairment in orientation, recent and remote memory, and was confused. The pyramidal tract signs on the left became more pronounced. He developed signs of a respiratory infection and died about three weeks after admission.

Post mortem examination showed a tumor in the region of the right basal ganglia, involving the caudate nucleus, the putamen, globus pallidus, and internal capsule, and extending into the corpora quadrigemina. A histologic examination was not carried out.

Comment. In this case the history of trauma was not confusing, mainly because it was considered rather trivial. A more severe trauma to the head would doubtless have resulted in greater diagnostic embarrassment. This was provided, however, by the history of long continued over-indulgence in alcohol. Since the tumor actually invaded the midbrain, it is apparent why a syndrome suggestive of Wernicke's polioencephalitis superior was produced. Here again, the sudden fulminating onset of symptoms in a case of tumor of the brain stem is noteworthy. Evidently the growth had remained dormant and asymptomatic for some time prior to this onset.

The following two cases are presented in this series, despite lack of pathologic confirmation, because the course during continued observation appears to indicate quite definitely the correct diagnosis. At any rate, they are valuable in focusing our attention on the difficulties involved in establishing such a diagnosis.

Case 4 (Adm. 404993). A messenger, aged 19, entered The Mount Sinai Hospital on March 29, 1935. At the age of fourteen he had been operated upon for osteomyelitis of the right os calcis, and had remained well since that time. Subsequently, during the course of the neurological examination, he ventured the opinion that the left side of his face had always been somewhat weak, so that he appeared to sneer when he smiled, and that his jaw had protruded toward the left. Three months before admission he suddenly developed altered sensation in the fourth and fifth fingers of his left hand, so that he was less able to recognize objects in that hand. He also noted awkwardness in performing skilled acts with that hand. Within two weeks, similar difficulties appeared in the right hand. Weakness was present in both hands. Three days before admission he saw double, and later in the day he had difficulty in closing the left eye, and the weakness of the left side of his face appeared more pronounced.

Examination. There was swaying in the Romberg test; ataxia in both upper limbs, astereognosis in both hands, position sense errors in both hands; vibratory sensation absent in both hands, diminished at and below the iliac crests; deep reflexes diminished in the upper limbs; there was evidence of a paralysis of the left sixth nerve and of the left seventh nerve, with gustatory sensation intact; the jaw deviated slightly to the left; there was nystagmus on gazing to the right and a nerve type of deafness on the left side. The fundi were normal; on one occasion there was contraction of the visual fields for red objects.

The cerebrospinal fluid showed a pressure of 130 mm. of water. There were 28 mononuclear cells. The colloidal gold curve was 5554320000. Serology was negative. The total protein was 50 mg. per 100 c.c. A biopsy of the nasopharynx was negative.

The earliest impression was that the patient was suffering from disseminated sclerosis, with lesions in the brain stem, cerebellar pathway, and possibly, the parietal lobes. The colloidal gold curve was of the type found in multiple sclerosis. However, there were certain features which were atypical of multiple sclerosis. The pyramidal tracts, which are usually the site of predilection for the lesions of multiple sclerosis, were spared. Also, the presence of the facial paresis of the lower motor neuron type, a rare condition in multiple sclerosis, was unusual. The question arose whether it was not possible to account for all the neurologic signs on the basis of a single lesion in the brain stem, rather than on the basis of disseminated lesions. A lesion involving the nucleus of the sixth nerve and the fibers of the seventh nerve winding around it, the medial lemnisci, the vestibular nuclei, and, perhaps, the acoustic nucleus on the left could account for the signs observed. The lesion might be a glioma or a syrinx. If the process affected the wall of the ventricle, then even the type of colloidal gold curve found could be accounted for.

Course. The patient was treated intensively with radiotherapy to the brain stem on the chance that this might be a neoplasm. Under this regime he improved definitely. The function of the sixth and seventh nerves became better, and there was improvement in vibratory and position sense in both hands. During a period of observation in the Follow-Up Clinic, the improvement appeared sustained. However, on February 23, 1937 the patient had to be readmitted to the hospital. He stated that in November, 1935, he had suffered from difficulty in recognition of objects with the right hand and inability to write or handle objects. After a period of about six months this condition had improved and remained so for another six months. Two weeks ago he was suddenly unable to distinguish objects with his left hand, and the right became worse in this respect.

Neurological Status. There were diminished swing of the right arm; slight ataxia in the lower limbs, and more marked ataxia in the upper limbs; dysidiadochokinesis.

Skilled acts were clumsily performed. Pseudo-athetoid movements of the fingers were present. The deep reflexes in the upper extremities were depressed; the abdominal reflexes were absent. There were bilateral Chaddock signs. The vibratory sense was impaired in the upper and lower limbs; position sense was impaired in the hands and feet. Bilateral astereognosis was present. The evidence of left sixth and seventh nerve palsy persisted. There was nystagmus on gazing to the right. The caloric responses and visual fields were normal. The spinal fluid showed ten lymphocytes, with negative serology and colloidal gold curve.

The diagnosis of multiple sclerosis was now considered more probable. However, the patient was given, in addition to typhoid therapy, radiotherapy to the brain stem and cervical spine.

When observed in the Follow-Up Clinic in August, 1937 the patient was complaining of difficulty in walking. His status was essentially unaltered.

Comment: The diagnostic problem which confronted observers when the case was first studied has been discussed in some detail above. No definite conclusion could be drawn at that time as to whether the case was one of multiple sclerosis or of a brain stem neoplasm, or syrinx. For a time the favorable response to radiotherapy might have seemed to confirm and strengthen the arguments in favor of a neoplastic process. However, the possibility of a spontaneous remission in the course of multiple sclerosis always looms up. Moreover, the longer the duration of the disease—now almost two and a half years—without significant progression, the less likely does the diagnosis of a brain stem neoplasm become.

Case 5 (Adm. 392061). A housewife, aged thirty-seven, was admitted to The Mount Sinai Hospital on April 16, 1936. The family history was irrelevant. Ten years ago, during a pregnancy, the patient had developed a cough; an X-ray examination of the chest taken at that time proved negative. Three years before she had been operated upon for an adenoma of the thyroid. She had been subject to frequent headaches over a number of years. Three weeks before admission the patient felt weak, with general discomfort and malaise. A week later she became nauseated. At about the same time her left hand felt "as though there were sand in it". The following day there occurred headache, nausea, and vomiting; her left limbs became paretic and the left side of the face appeared distorted. The headache, nausea and vomiting recurred during the following two weeks. Diplopia occurred. Shortly before admission she began to suffer from burning sensation in the head, dysphagia and alterations in voice.

Examination. The patient, who was bedridden, appeared acutely ill and torpid. There was tenderness over the left antrum and a purulent nasal discharge. The tonsils and fauces were injected. The pulse was 72, the blood pressure was 100 systolic and 70 diastolic.

Neurologically, there were ataxia of the left upper and lower limbs, and, to a slighter degree, of the right lower; adiadochokinesis of the left upper limb. The speech was slow and nasal in quality. There was moderate left hemiparesis with pyramidal tract signs. The abdominal reflexes were absent bilaterally. Vibration sense was diminished in the left limb; position sense was lost in the left foot, hand, wrist, and elbow joint, two-point discrimination was impaired in the left hand, as were touch localization and stereognostic sense. There was questionable diminution of cutaneous sensation over the left side of the body. Diplopia was elicited in all directions with the red glass test. Conjugate gaze to the right was impaired; con-

vergence of the left eye was impaired; and upward movement of the left eye was incomplete. There was a left external strabismus; vertical nystagmus was present on upward gaze and horizontal nystagmus on gaze to the left. The left eyelid was ptotic. There was questionable weakness of the soft palate. Mentally, the patient was drowsy, querulous, emotionally unstable, with occasional lapses into facetiousness.

The blood count was normal. The blood Wassermann was negative. The cerebrospinal fluid was under a pressure of 60 mm. of water, slightly xanthochromic, and contained four mononuclear cells per cubic millimeter. The Pandy test was negative, as was the Wassermann. Caloric tests were unsatisfactory, because of the ocular palsies. Sinus examination disclosed bilateral ethmoiditis.

The diagnoses considered were: encephalitis; acute multiple sclerosis; vascular disease of the pons, chiefly in the distribution of the posterior inferior cerebellar artery; and brain stem neoplasm.

Course: The patient was given typhoid vaccine therapy. Her neurological status improved definitely during the next few weeks. The ataxia and the left hemiparesis persisted, as did the sensory disturbances, but the ocular movements became normal; only vertical nystagmus remained, and there was no longer any ptosis.

Nevertheless, because of the possibility that there might be a neoplasm of the brain stem, she was given radiotherapy. About seven weeks after admission a neurological status showed that the improvement was sustained.

A subsequent examination in the Follow-Up Clinic about six weeks later showed but few residual signs. The patient was ambulatory. Her gait was somewhat broad-based. There were no objective sensory changes. Motor power was normal, although the deep reflexes on the left side were somewhat increased. There was still slight ataxia in the left upper limb. The ocular movements were normal. Mentally, the patient appeared depressed, and stated she was troubled by compulsive ideas that she might murder those dearest to her. She refused treatment in the Mental Health Clinic and failed subsequently to report to the Follow-Up Clinic.

Comment: From the variety of opinions suggested, it is quite apparent that the diagnostic problem was not a simple one. Encephalitis, acute multiple sclerosis, vascular disease of the brain stem, and neoplasm of the brain stem were each considered, indicating doubt not only as to the nature of the pathological process but also as to its localization. Vascular disease of the brain stem did not appear very likely in the absence of lues or generalized arteriosclerosis, and in view of the fact that the structures involved did not lie in the distribution of any one vessel, such as the posterior inferior cerebellar, superior cerebellar, or anterior spinal artery. The differential diagnosis lay rather between an inflammatory and a neoplastic process. The suddenness of onset, with evidence of infection in the upper respiratory tract, were in favor of the former; the absence of pleocytosis in the spinal fluid is not inconsistent with such a diagnosis. On the other hand, we have learned that brain stem neoplasms may announce themselves clinically very abruptly. It is unfortunate that the patient proved uncooperative in attending the Follow-Up Clinic. As matters stand, with improvement maintained for a period of some three months, an encephalitic process appears the more likely diagnosis. Since the distinction between an encephalitic process and acute multiple sclerosis may be

a source of contention between pathologists, even after histologic study, it need not be further discussed in a clinical presentation.

SUMMARY

Some of the difficulties inherent in the diagnosis of brain stem syndromes were illustrated by means of a small series of representative cases. It has been shown that neoplasms in this region may prove deceptive, when the onset is acute and fulminating, as in inflammatory disease, and when the course is interrupted by remissions. Attention was directed to the difficulty of establishing, in certain cases, whether a group of neurologic signs is to be attributed to disseminated lesions or to a single, discrete lesion in the brain stem, incriminating nuclear structures and the long pathways. The great disparity that may exist between the extensiveness of a brain stem tumor and the few, or absent clinical signs manifested up to a certain time, has been pointed out, suggesting the relative invulnerability of these structures to pressure. Syndromes due to occlusion of a blood vessel should offer but little difficulty because of the fairly constant involvement of the same structures in any case of any particular vessel involved. The difficulty will arise more often in distinguishing between an inflammatory and a neoplastic disease, or between the latter and multiple sclerosis. Increasing experience with such cases should sharpen one's diagnostic acumen; but there will undoubtedly remain cases which will prove baffling to the most astute clinician, and in which only more prolonged observation will serve to clarify the problem.

HYPEROSTOSIS FRONTALIS INTERNA AND DEGENERATIVE BRAIN DISEASE*

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Since Stewart (1), in 1927, and Morel (2), in 1929, noted the common association of groups of symptoms with hyperostosis of the internal table of the frontal bone several writers in this country have made contributions to the subject. Moore (3, 4) and Carr (5) have called attention to neuropsychiatric and metabolic syndromes, vaguely defined because of the variability in symptomatology, which they cannot account for on the basis of the hyperostoses alone. They infer that metabolic factors may account for both the osseous and the neuropsychiatric disorders. Over 98 per cent of the patients with these hyperostoses are women; the majority of them are obese and suffer from menstrual disorders. Headaches, weakness, dizziness, memory defects and convulsions are the most striking symptoms. The psychiatric pictures vary widely from simple memory defects to syndromes of senile psychosis.

The variable, and in general vague, nature of the psychiatric accompaniments to the disturbance in the calvarium presents the reason for the following two case reports. In the one case there was associated with the hyperostosis a quite definite neuropsychiatric syndrome, proved by post mortem studies to be Alzheimer's disease, and in the other a clinical syndrome less clearly defined, yet having the appearance of a post-traumatic personality disorder with petit mal attacks. Both patients were women.

REPORTS

Case 1. History. The patient was a 55 year old married woman whose family and past histories were irrelevant. With the exception of a hysterectomy for a fibroid tumor at the age of 33, her health was good until the onset of the present illness. She had never become pregnant.

Three years before admission she began to fatigue easily, became nervous and lost about twenty pounds in weight. A few months later she noted with considerable embarrassment that she was frequently at a loss to use words to express herself. Within the past year she had lost the ability to tell time or to know the day of the week. Her orientation for place and person remained good. For several months she complained of a severe headache behind her left eye, and at the bridge of the nose. Slowly and gradually her symptoms became worse so that she became unable to understand what she was reading and could no longer write her own name. Her inability of expression became so marked that on going shopping she would select what she wanted by pointing. The headaches increased in frequency and severity.

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Physical Examination. The patient was fairly well developed and well nourished, despite her loss of weight, indicating that prior to the onset of her illness she might have been considered obese. A few psoriatic patches were present on the forehead at the hairline. The eyeballs were prominent and a positive von Graefe sign was demonstrable. Heart and lungs were normal; blood pressure was 140 systolic and 78 diastolic, pulse was 88 per minute. Other findings were a low midline abdominal scar, an atrophic vagina and marked hirsutism over the legs. No skull tenderness was present.

Neurological Examination. The only abnormal neurological findings were the aphasic manifestations. The patient's speech exhibited repetition, perseveration, elisions and neologisms. She could not name objects but could demonstrate their use satisfactorily. She handled a pencil clumsily, but did well with comb, knife and fork. Simple commands she followed well, but a double command left her perplexed. For instance, when asked to open her mouth or close her eyes she obeyed correctly, but when asked to do both together she could not. She made errors in reading and gave no indication of understanding what she read, for simple commands, such as she would follow verbally, were ignored when written. A marked dysgraphia existed. The patient could tell right from left but made frequent errors in imitating the position of the examiner's fingers. She could hum simple tunes but could not sing the words.

Mental Examination. The patient was somewhat distressed by her inability to express herself. At times she was moved to tears. Most of the time, however, she was pleasant and even euphoric. Her memory was difficult to test because of the impairment of speech; disorientation for both time and place was now evident. Simple calculation was faulty. She was restless, especially at night, and wandered around the halls a good deal. Wherever she went she took with her a large handbag which contained nothing but her spectacle case.

Laboratory Examination. The urine and blood showed no abnormalities. The Wassermann test was negative. Lumbar puncture yielded clear, colorless spinal fluid at a pressure of 100 mm. of water. The cell count was six and the total protein 48 mg. The spinal fluid Wassermann and colloidal gold curve were negative and the basal metabolic rate was minus 10 per cent. Roentgenographic examination of the skull showed an irregular, rounded shadow of uneven density in the left frontal region. In some views this shadow appeared trabeculated. At the time of the initial study of the case consideration was given to the diagnosis of a hyperostosis.

From the examination the tentative diagnosis of Alzheimer's disease was made, but, in view of the localized and progressive headache and the left frontal shadow on X-ray examination, an encephalogram was recommended and carried out on August 14, 1935. The findings were those of a mild internal hydrocephalus. In addition, there were some areas of air over the cortex suggesting cortical atrophy (Fig. 1).

Five days after the encephalogram the patient left the hospital somewhat more euphoric than on her admission. For two months her relative euphoria continued, but later it was reported that she was becoming more confused, depressed, and was almost completely speechless. She became bed-ridden, incontinent, and died at her home three months after leaving the hospital.

Post Mortem Examination (Limited to cranial contents). On removal of the calvarium a large mass of bluish purple hyperostosis was found in the left frontal and temporal regions. Their extension was much greater than was indicated on the X-ray plate, suggesting that a great deal of growth had taken place in the last few months of the patient's life. The hyperostoses covered an area of about four centimeters square, arose from the inner table of the skull, and consisted of cancel-

lous bone, nodular in shape, extending inward toward the brain for distances varying from a few millimeters to 1.5 centimeters. The group in the temporal region was somewhat separated from the larger frontal mass.

The meninges were normal and there was no thickening in the area of the hyperostosis. The brain was pale, small and very firm. The left frontal lobe was considerably smaller than the right because of indentations, caused by pressure of the hyperostoses, and slight indentations were present compressing the anterior pole of the first and second left temporal convolutions; these latter were caused by the temporal hyperostosis previously mentioned. The gyri were small. The vessels at the base were mildly sclerotic. On cut section a moderate internal hydrocephalus was present. Despite the pressure effects on the brain caused by the hyperostoses there was no displacement or distortion of the ventricular system. In many areas the cortex was very thin.

Microscopic preparations were made, using hematoxylin-eosin, Bielschowsky and Hortega silver impregnation methods, Spielmeyer, Nissl, Scharlach R., Cajal gold

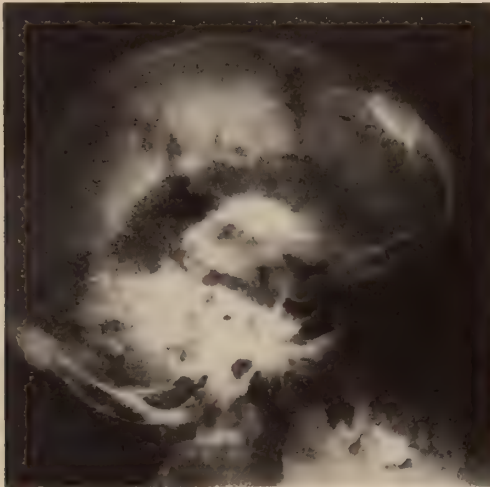


FIG. 1. Lateral X-ray picture of the skull following encephalography in Case 1.

sublimate and Holzer methods. Over the left frontal lobe, left hippocampus and cerebellum the pia arachnoid was thickened and laden with histiocytes. There was marked hyalinization of numerous blood vessels throughout the brain with perivascular round cell infiltration of some vessels. With the silver impregnation methods neurofibrillar thickening could be seen. Senile plaques were very common throughout the cortex of the left frontal region and left hippocampus. Some of these plaques appeared as granular masses and others as agglomerations of degenerating ganglion and glial cells (Fig. 2). Occasionally marked distortion of the architecture of the cortical lamina was seen. There were occasional fatty deposits, and these only in the adventitial spaces of the smaller vessels. Small areas of demyelination were noted in the subcortex of the left frontal lobe and both internal capsules, but these were not prominent. The wall of the third ventricle, mentioned by Morel to be the site of granular degeneration of a type characteristic of hyperostosis, and thought by him to be indicative of derangement of calcium regulating centers, in this case showed no unusual changes.

The changes in the pituitary were restricted to the anterior lobe. The acidophile was the most numerous cell type. The basophiles were larger than normal, had irregular shapes, enlarged nuclei and frequently two nuclei. There were large numbers of hypertrophic chromophobe cells, having a granular cytoplasm, which in the majority of cells did not stain with aniline blue, but which, in some cells, took a faint basophilic tint. There was a slight amount of colloid retention and no increase in the stroma. The observations on this pituitary differed greatly from the observations made by Stewart, who found an excess of connective tissue in the cases he studied. Dr. Charles Spark (Montefiore Hospital, New York City), who has studied these sections, concluded that the pars anterior in this case shows evidence of "activity."

COMMENT

It would be idle speculation to try to link the Alzheimer's disease and the hyperostosis to a common etiologic factor. But, considering them as

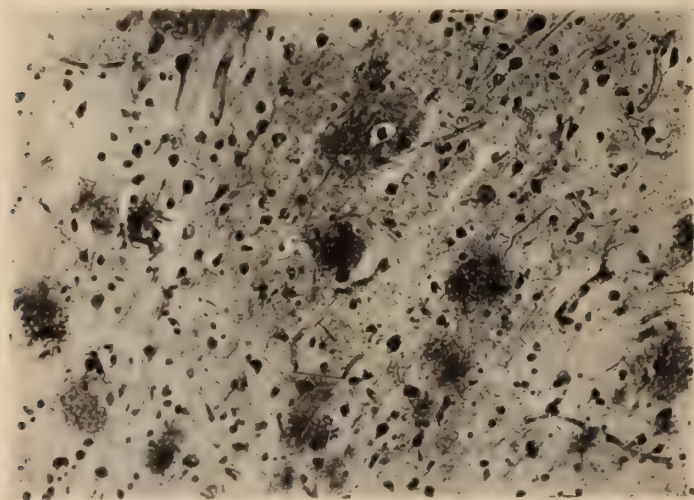


FIG. 2. Photomicrograph of left frontal cortex in Case 1, showing findings characteristic of Alzheimer's disease.

coexistent entities, we see, first of all, that early in this patient's life there occurred some metabolic and uterine dysfunctions. How much the hyperostoses were a factor in this endocrine derangement, or even whether they existed then, no one knows. However, they were probably the cause of the patient's headaches in her presenting illness, and finally, they may have aggravated her mental symptoms. The morphological effect of the pressure they exerted on the left frontal lobe is evident, yet the aphasia seems quite definitely due to the Alzheimer's disease. It is not necessary, in view of the microscopic findings, to invoke the hyperostoses as explanations of the entire neuropsychiatric picture.

Case 2. History. The patient was a 40 year old married woman who had had menstrual irregularity ever since the onset of her menses at the age of 11. Fourteen

years previously, at the age of 26, she had had a very severe head trauma in an accident, which was followed by a period of unconsciousness of several weeks' duration. After regaining consciousness she had had headaches for six months. A change in personality was then noticed. She became selfish, malicious, and very compulsive. At the age of 28 she became married. She had two miscarriages and one tubal pregnancy. Three years ago, at the age of 37, she became fatigued, and several months after that she began to have numerous petit mal attacks. During the past year she had had a poor memory for recent events. She had been studied by competent neurologists who noted a hyperostosis in the frontal region, and who, following Carr's suggestion, have given her large quantities of aminoacetic acid in the form of gelatine sheets. These did not alter her symptoms at all.

Physical, neurological and laboratory examinations yielded no pathological findings. On mental examination the character disorder was evident, and likewise the loss of memory for recent events. Encephalography (Fig. 3) was performed, which showed an increase in air over the cortex, indicating a mild cortical atrophy.

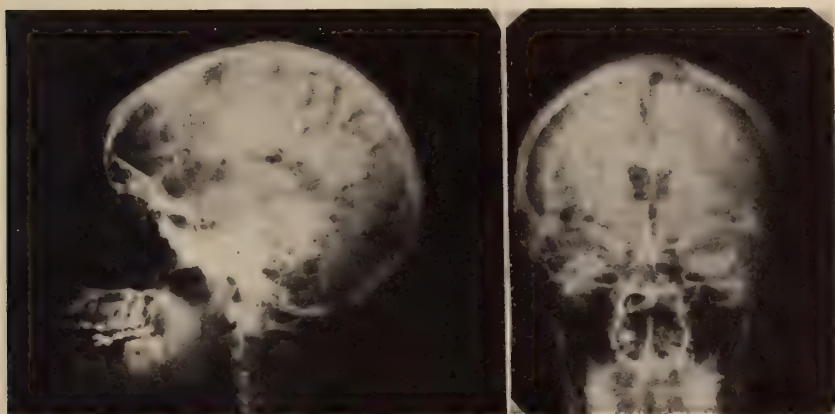


FIG. 3. Encephalogram in Case 2, showing cortical atrophy

Comment. Here again, if one wishes, he could correlate the entire psychiatric picture with the old history of head injury, even though the trauma occurred over ten years previously. However, the clinical syndrome fits very nicely into the category of neuropsychiatric accompaniments of the hyperostosis. Furthermore, Schiff and Trelles (6) have described a case of hyperostosis with cerebral complications which followed a head injury.

Even though in these cases the pathogenic factor of the craniopathy is a debatable one, it is important to point out that review of the neuropsychiatric cases associated with this osseous disorder hitherto reported, demonstrates syndromes of organic mental disease, and I believe, as a result of our studies, that the organic change is a degenerative one. Hence, in the future, study may divulge that a closely knit relationship may exist between these two sets of findings. If Mortimer's (7) contention that calvarial hyperostosis is due to hypopituitarism be sustained, the question

of the mechanism of the possible effect of the endocrinopathy on degenerative disease of the brain is brought to the fore.

SUMMARY

The association of hyperostosis frontalis interna with degenerative brain disease is noted in two cases. The rôle that the hyperostosis played in the production of the clinical picture is discussed and is thought in these instances to be only of contributory etiologic importance. Nevertheless, the coexistence of the craniopathy in neuropsychiatric and endocrinopathic syndromes seems not to be due solely to chance and there appears to be a definite, though, as yet, obscure, relationship.

From the clinical-pathological point of view it is important to stress that the cerebral changes are of a degenerative nature.

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SENILE CHOREA AND ITS RELATION TO HUNTINGTON'S CHOREA

REPORT OF A CASE

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Among the cases of chronic chorea occurring in adult life and running a progressive course there is a small group without hereditary or exogenous features to which the term senile chorea has been applied. This term was meant to designate a condition based on senile changes and not merely a variety of choreic pictures falling by chance in the senile period of life.¹ Nevertheless, different conceptions of the disorder have been advanced by different writers and doubts as to its very existence have been expressed.

According to Alcock (1), it is a chronic chorea coming on in late middle life without mental changes and without a family history of chorea. Jakob (2) and the German authors in general regarded it as a symptomatic chorea occurring as part of the more widespread senile processes associated with senile dementia. Even when the term is used in this broader sense, senile chorea is a rare disorder. Apparently the first histologic reports appeared in 1923, when Jakob and Leyser (3) each described a case. Peter (4) reported one case in 1924, and since that time two cases have been described by Meyjes (5) and a similar number by Alcock. Dunlap (6) and others have made casual references to the subject, but they failed to provide sufficient data to be of distinct value. Kehrer (7) suggested that some cases of senile chorea really belonged to the group of cases of Huntington's chorea with a late onset. Peter found that the two disorders could not always be differentiated from one another on clinical or pathologic grounds, and he therefore doubted whether there was any justification for regarding senile chorea as an independent entity.

In view of these differences of opinion, a closer investigation of the whole subject is indicated. From a survey of the literature, one gains the impression that a diagnosis of senile chorea has been made largely because of a lack of conformity to the classical picture of Huntington's chorea, and not because of any positive features pointing to senile influences. The question arises:—Are there cases which present such features and, if so,

¹ The term "senile" has occasionally been used for cases of chronic chorea based on arteriosclerotic changes, but from a histologic viewpoint this term should be restricted to the well known parenchymal changes which are apparently independent of primary vascular involvement.

what is their significance? The following case may perhaps throw some light on this problem.

History. R. B. H., a married man, aged 67, was admitted to the Foxborough State Hospital on August 14, 1929. The patient was of English descent and his ancestors were among the earlier settlers of Massachusetts. The family history was not entirely satisfactory owing to the fact that no contemporary blood relatives of the patient were available. According to the wife, who seemed fairly well informed, there was no history of mental disease in the grandparents. The mother, who was normal mentally, died at the age of 70 of "fat around the heart." The father was a successful business man who retired at the age of 50 in order to let his sons carry on the business. He died of Bright's disease at about the age of 70. He was a nervous, restless man who became more nervous and restless during the last years of his life, but it was not thought that he had shown distinct mental changes or choreic movements. The patient was the fourth of six siblings, the two youngest of whom died in infancy of unknown causes. The oldest sibling, a brother, had moved many years ago to a distant state, where he died suddenly in the sixties, probably of "heart failure" or "apoplexy." The second sibling was a brother who died suddenly in the early seventies, apparently of "heart failure." He was described by a son-in-law as "a bit off." This sibling had a daughter who suffered from dementia praecox, but there was a history of mental disease on the maternal side of her family. The third sibling, a sister, aged 70, was thought to be still living; she had not been in direct contact with the family for many years. According to the patient's wife, all the siblings were of a "nervous temperament," but they did not exhibit mental changes or abnormal motor phenomena. However, the patient stated in a casual manner that his father, oldest brother and sister had shown twitching movements identical with those from which he himself suffered.

The patient was an unruly child and presented conduct disturbances throughout his school life. At the age of 13 he received a head injury after which he was "nearly paralysed." He finished high school and attended an agricultural college but was expelled in a few months owing to unruly conduct. He was married and had had six children. The oldest, a daughter, aged 40, has been diagnosed as feeble-minded by the family physician. A daughter died of pneumonia at the age of 11. A son, aged 29, was regarded as eccentric and "not very bright." The other children and the wife were normal. There was no history of mental illness in the wife's family. The patient worked for his father, who owned a factory. After his father's death, the patient established a factory of his own; this venture was a failure. He bought a large farm, which proved fairly successful, but gave it up and bought some property on which he lost a good deal of money. Another farming venture was a failure. For the past ten years the patient had had no regular employment, working in temporary positions of a simple nature. He had been totally unemployed for four years previous to admission to the hospital. He was always considered to be of a "nervous temperament." He was described as "bossy," "a difficult personality," optimistic, with strong likes and dislikes. He was a fairly good mixer, fond of sports and reading. He had always caused friction in the family by interfering with the plans of his children and objecting to their social activities. His present illness began very insidiously after the age of 50. For many years the chief feature was a gradually increasing accentuation of his unpleasant personality traits. It was thought that he began to show irregular twitching movements about ten years prior to admission, but for many years they were so slight that they were scarcely noticeable. During the past three or four years the motor symptoms and mental changes became more pronounced. He grew more irritable and quarrelsome, constantly criticizing his children's behavior. He accused his wife of encouraging the

daughters to stay out late with men, and on one occasion he attempted to choke her. He became very suspicious of his children's friends and was antagonistic toward them. He accused his wife of being insane and finally became so threatening in his attitude towards the family that it was necessary to commit him to the hospital.

Examination. The patient was a well developed and well nourished elderly looking man with gray hair. The blood pressure was 160 systolic and 80 diastolic. The retinal arteries were slightly tortuous. The patient showed constant choreic movements which involved all parts of the body, including the face and head. They were most marked in the upper extremities. They could be partially controlled for short periods but became more pronounced under emotional stress. The speech was jerky and explosive. The muscular tonus varied from moment to moment, but there was no constant hypotonia or hypertonia. The neurological examination was normal in other respects. The patient was jovial and mildly elated. There was slight impairment of memory for finer details and his grasp of general information was slightly defective. He suspected that his wife had hypnotized the children, causing them to turn against him. He had no insight and his judgment was poor. When asked about the choreic symptoms he said, "Those little things, they don't amount to anything."

Laboratory Data. Examinations of the urine and blood yielded normal results. The Wassermann reaction of the blood was negative.

Course. The patient soon became antagonistic and sarcastic towards the hospital employees. He used a good deal of profanity. He was very antagonistic towards his wife and children, accusing them of cunning and treacherous behavior and of "framing" him. He constantly suspected that the nurses were discriminating against him. There was no definite change in the choreic symptoms. It was impossible to interest him in any occupation. In April, 1931, it was noted that the patient occasionally attacked other patients. He explained these acts as follows: "They talk about me indirectly, a mental influence, stronger than the mind. It is a sort of species of hypnotism. They just get into my mind. They put words into my mouth and I speak them out." This type of behavior continued during the following year. On one occasion the patient stated that someone was controlling his mind by mental telepathy. He accused some patients of trying to make him become a sexual pervert. The choreic movements gradually grew more marked, and there was considerable loss in weight. He showed increasing mental deterioration. In June, 1932, it was noted that many of his replies to questions were irrelevant. He spent a good deal of time talking out the windows, apparently to imaginary persons. On January 2, 1933, he developed a slight cough with a temperature of 103°F. He was kept in bed for seven days. During this period he was restless, noisy and incontinent. He seemed to make a good recovery but had a weak spell on January 23, 1933. He was extremely confused. He gradually grew weaker and died on January 30, 1933.

Gross Pathologic Findings. Necropsy was performed eighteen hours after death. There was a moderate amount of clear fluid in the pleural cavities. The lungs were edematous. The heart weighed 375 gm. and the muscle was pale and flabby. The coronary arteries showed a few small yellowish plaques. The gall-bladder contained one small stone. The prostate was enlarged and the bladder was distended. There was dilatation of the ureter and pelvis of both kidneys. The pia-arachnoid was slightly opaque. The brain weighed 1475 gm. The basal vessels of the brain were delicate. On section, the lenticular nuclei appeared smaller than normal, and the lateral ventricles were slightly dilated.

Microscopic Findings. The pia-arachnoid was thickened in places, showing many fibroblastic cells, frequent histiocytes and occasional macrophages. Very slight

intimal thickening was observed in a few of the larger blood vessels. Some of the small meningeal vessels presented moderate thickening and a hyaline appearance of their walls. The vessels of the choroid plexus showed severe but spotty adventitial proliferation.

The cerebral cortex showed a diffuse loss of nerve cells, which was most marked in the frontal and precentral regions (Fig. 1). The parietal lobe presented moderately severe involvement and the temporal and occipital lobes relatively mild changes. The damage was usually greatest in the third layer, though all layers were affected. Pronounced disturbances of the cyto-architecture were not noted. In the severely involved areas the nerve cells were pale, the Nissl bodies were indistinct or absent and cell shadows were common. Many of the Betz cells exhibited changes of this type. In the cornu ammonis, a few small pale areas were observed and a small portion of Sommer's sector was completely softened. The Dieterle-

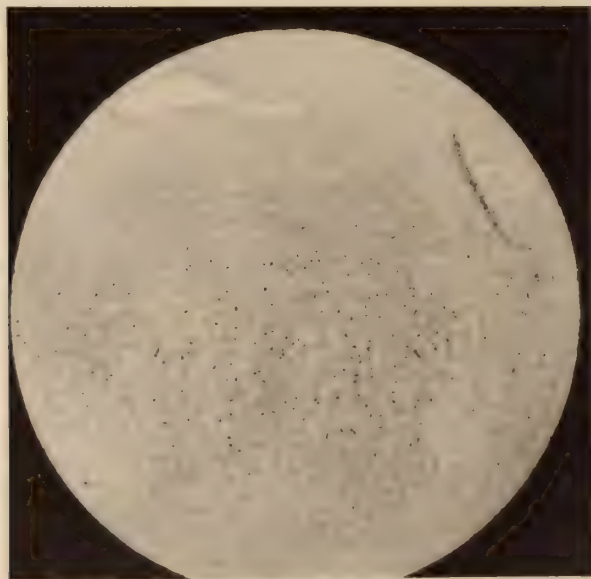


FIG. 1. Section from the anterior frontal region showing diffuse loss of nerve cells without pronounced disturbances of the cyto-architecture. Thionin stain; $\times 35$.

Neumann modification of the Hortega stain disclosed senile plaques in all parts of the cerebral cortex (Fig. 2). As a rule they were present in small numbers, most areas exhibiting from five to fifteen plaques per low power field.² Some of the plaques were pale and indistinct, giving the impression of "young" forms, but many were large and clear-cut. Neurofibril alterations of the Alzheimer type were not encountered. There was diffuse proliferation of microglia cells in the form of large rod cells and irregularly shaped elements. Throughout the cerebral tissue the astrocytes were increased in number. This was especially pronounced in the subcortical white matter (Fig. 3).

The capillary network of the cerebral cortex appeared unusually prominent in sections treated with silver stains. In the cortex and white matter the precapillaries showed marked adventitial and endothelial proliferation. The vessels of

² The plaques were counted with a Zeiss binocular microscope, objective 8, numerical aperture 0.2, ocular $\times 10$.

the white matter were often engorged with blood, and dilatation of the perivascular spaces was common.

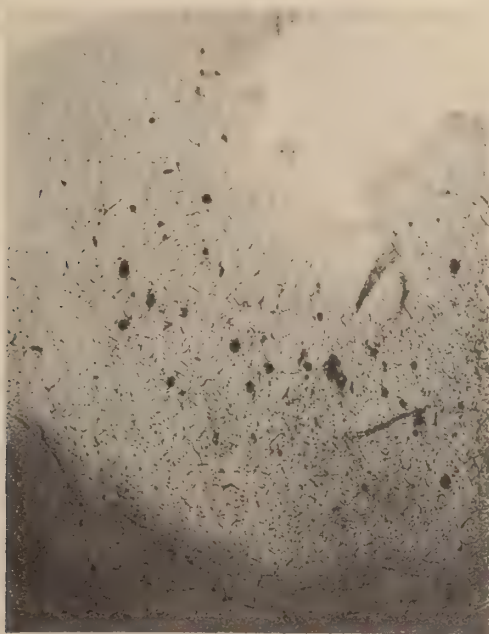


FIG. 2. Section from the cerebral cortex showing a small number of senile plaques, which appear as rounded, darkly stained areas. Dieterle-Neumann modification of the Hortega stain; $\times 27$.

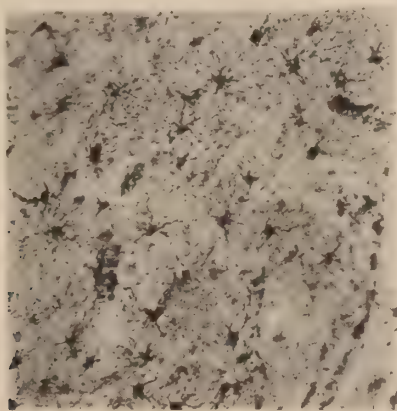


FIG. 3. Section from the subcortical white matter showing marked astrocytic proliferation. Cajal's gold sublimate stain; $\times 215$.

The caudate nucleus and putamen showed a marked paucity of small nerve cells (Fig. 4). The loss of cells was diffuse but varied considerably in severity from place to place, even in closely adjacent parts. On the whole, the changes were more

pronounced in the putamen than in the caudate nucleus. In some places very few small neurones were preserved and the remaining cells were pale and shadowy. The large nerve cells were not noticeably decreased in number (Fig. 4). In some fields they actually seemed to be more abundant than usual. However, most of them were abnormal in appearance. They were irregular in shape and pale, and many of them were colored by the Nissl stain in an uneven manner. In the inner portion of the putamen there were numerous globules of pigment, which appeared black in the Nissl, hematoxylin-eosin, van Gieson and silver stains and pale blue in sections stained by the Turnbull blue method for iron. Most of these globules were located in the perivascular spaces but some were lying free in the tissues. There was a pronounced increase of neuroglial elements, which sometimes gave an

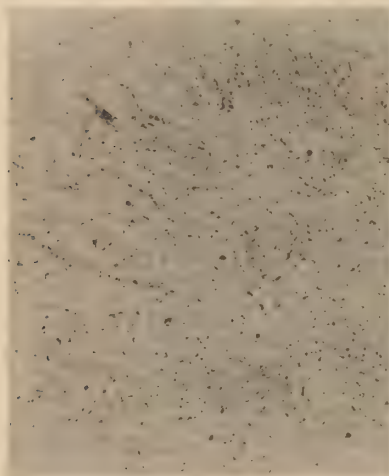


FIG. 4

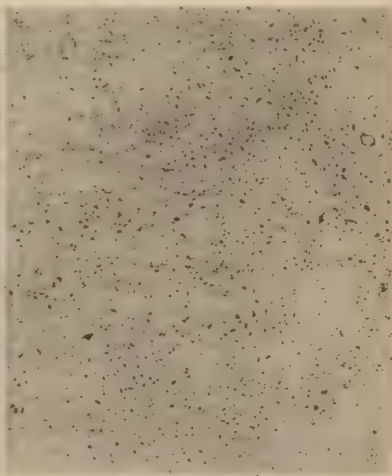


FIG. 5

FIG. 4. Section from the putamen. The small nerve cells are pale and indistinct and greatly diminished in number. The large nerve cells are not decreased in number but many of them are poorly stained and hazy. There is diffuse neuroglial proliferation which gives an impression of cell richness despite the marked paucity of small neurones. This section should be compared with a corresponding section from a normal brain in Figure 5. Thionin stain; $\times 52$.

FIG. 5. Section from the putamen of a normal brain. The small nerve cells here are more abundant and better preserved and the glia cells are less numerous than in Figure 4. Thionin stain; $\times 52$.

impression of cell richness in areas where the nerve cells were very scanty in number (Fig. 4). These features are well demonstrated by a comparison with a section from the putamen of a normal brain illustrated in figure 5. With the Dieterle-Neumann modification of the Hortega stain, numerous senile plaques were observed in the putamen and caudate nucleus (Fig. 6). Most areas showed from twenty to thirty-five plaques per low power field, though small numbers were not uncommon and a few low power fields failed to contain these structures. The plaques were most abundant in the outer portion of the putamen (Fig. 6). The smaller vessels exhibited pronounced proliferative changes. Occasionally a few lymphocytes were seen in the perivascular spaces.

In the globus pallidus the nerve cells appeared closer together than usual, but the

whole nucleus seemed decreased in size. In sections stained with thionin the nerve cells often showed considerable amounts of yellowish pigment. There was diffuse neuroglial proliferation. The other basal nuclei failed to present noteworthy alterations. The cerebellum showed a small area of softening occupying several low power fields. Elsewhere in the cerebellum the Purkinje cells were pale, but they were not distinctly diminished in number.

Comment. In spite of the late onset, prolonged course and lack of clear-cut family history of chorea³, there were many clinical features in this case suggestive of Huntington's chorea. The patient's personality, which was characterized by unruly, unstable and irritable traits, was similar to the type of make-up frequently attributed to persons who de-



FIG. 6. Section from the putamen showing an abundance of senile plaques, which are scattered in a somewhat irregular manner throughout the nucleus. The outer margin of the putamen is visible in the upper left hand corner of the figure. Dieterle-Neumann modification of the Hortega stain; $\times 27$.

velop Huntington's chorea. As the disorder progressed, the paranoid tendencies of the patient grew into more outspoken persecutory ideas with angry outbursts and threatening behavior. Such a picture has been considered typical of psychoses with Huntington's chorea. The fact that two of the patient's children were abnormal mentally suggests a defective heredity. In this connection, it may be recalled that a variety of mental abnormalities without choreic symptoms have been observed by Daven-

³ The reliability of the patient's statement that three members of his family showed choreiform movements may be questioned, since it was unsupported by other observers. Unfortunately, it was not possible to undertake an independent investigation of the patient's relatives.

port and Muncey (8), Meierhofer (9), and others, in relatives of patients with Huntington's chorea. It might also be pointed out that the mental disorder in the present case bore little resemblance to a senile psychosis; in particular, the lack of outspoken intellectual deterioration until the terminal stages of the illness would be highly unusual in senile dementia.

Histologically, the most striking feature was the occurrence of senile plaques in the cerebral cortex and striatum. Apart from this, the alterations were similar to the changes generally associated with Huntington's chorea. The proliferative lesions of the small vessels were perhaps more marked than usual, but tissue changes that could be attributed to vascular involvement played no significant rôle in the pathologic picture.

To my knowledge there have been no reports of typical cases of Huntington's chorea with senile plaques in the brain. Even in the cases diagnosed as senile chorea, plaques have not been found in the striatum. They have also been absent from the cerebral cortex in some instances. This is surprising, for it is now generally believed that such lesions of the cortex are closely associated with pathologic aspects of senility. However, the frequency of occurrence of plaques in the basal ganglia has been a subject of considerable dispute. Boumann and Bok (10) claimed that these alterations were present in the striatum in almost all cases of senile dementia, whereas Grünthal (11) and others believed that they were usually lacking. Dunlap remarked that the caudate nucleus and putamen were often loaded down with plaques in senile dementia, but he gave no actual figures on the subject. Gellerstedt (12) studied fifty elderly persons who were normal mentally and found plaques in the putamen in fifteen cases. My observations are in accord with those of Boumann and Bok, a recent investigation (13) disclosing the lesions in the striatum in eighteen* of twenty cases of senile dementia. Boumann and Bok suggested that the failure to obtain positive results more frequently might be due to faulty fixation of the centrally located striatal structures. Another probable cause of conflicting results is that the newer silver stains are more sensitive and more reliable in revealing senile plaques than some of the older, commonly used procedures.

In the case reported here the putamen and caudate nucleus showed the greatest number of plaques. The degree of involvement of the cerebral cortex was not as pronounced as that observed in the average case of senile psychosis, but the lesions were more abundant in the putamen and caudate nucleus than in the corresponding parts of most of the senile brains previously studied (13). In one or two cases of Alzheimer's disease (14), the striatum exhibited equally severe damage. To my knowledge, however, no cases have been reported in which plaques were much more abundant in the basal ganglia than in the cerebral cortex.

The fact that the senile plaques were distributed in this unusual manner, which corresponded to the distribution of the cellular involvement,

strongly suggests that they were an integral part of the whole pathologic process. It might be argued that they occurred with greatest abundance in the striatum merely because that region was a *locus minoris resistentiae*. Against this argument one might point out that in elderly persons the basal ganglia are often severely damaged in various ways without showing any tendency to the formation of senile plaques. In view of these considerations, it is likely that the plaques were part and parcel of the pathologic process and not merely an extraneous complication.

GENERAL DISCUSSION

The foregoing observations demonstrate that a chronic and progressive form of chorea may be associated with a characteristically senile histologic picture. However, this does not necessarily mean that the disorder is genuinely senile in the sense that senescent influences are solely or even primarily responsible for its occurrence. It is well known (14) that the changes typical of senile processes occasionally crop up in conditions bearing no apparent relation to senility. These experiences have led to wide acceptance of the conception that such lesions are special manifestations of a general type of tissue reaction. Von Braunmühl (15) has studied the subject exhaustively, and it is interesting that he regarded Huntington's chorea as one of the non-senile conditions which exhibited this general type of tissue reaction. Even apart from his more or less speculative views, there is sufficient empirical evidence to indicate that the changes in question can no longer be looked upon as pathognomonic of any particular disease. The whole setting in which they occur, including clinical aspects of the picture, must be scrutinized before arriving at diagnostic conclusions.

There are considerable differences of opinion concerning the clinical picture of senile chorea. According to Alcock, the mere presence of a psychosis should exclude a case from the senile group. This view is open to serious objections. If the term "senile" as applied to chorea has any real significance it denotes a senile tissue process of a pathologic nature; this process may conceivably be limited to subcortical centers in some cases, but there is no reason why it should not be accompanied by pathologic senile manifestations elsewhere, for example in the cerebral cortex. The fact is, Jakob, Meyjes and other German writers took it for granted that the disorder occurred regularly within the broader framework of senile dementia and its associated mental disturbances. One is led to conclude that the presence or absence of mental changes can not be considered of distinct value in distinguishing senile chorea from Huntington's chorea. This conclusion gains support from another direction in the observations of Davenport and Muncey and others, which indicate that mental disturbances may be lacking in cases of Huntington's chorea.

In the case reported here, the mental disturbances resembled those

frequently depicted as characteristic of Huntington's chorea. Yet it is questionable whether the type of psychotic picture can be considered of decisive importance in differentiating between the two disorders, since the mental changes in both conditions are based on diffuse damage to the brain. A late onset is not of definite diagnostic value, for genuine examples of Huntington's chorea have been observed in persons of advanced age. Apparently the only feature which might clearly distinguish Huntington's chorea from senile chorea is the well established hereditary factor in the former. Unfortunately, a thoroughly reliable family history is often unobtainable. The diagnostic difficulties under these circumstances are well illustrated by the case of Peter, which was originally regarded as an example of senile chorea, though subsequent investigation disclosed the presence of chronic progressive chorea in members of the patient's family.

One of the features of senile chorea which calls for comment is its rarity. Judging from the literature on the subject, it occurs much less frequently than Huntington's chorea. This is surprising in view of the fact that senile changes are very common in the areas believed to play an important rôle in the production of choreic symptoms. Experiences with senile conditions (13) and Alzheimer's disease (14) have shown that senile chorea can not be attributed to simple quantitative differences in the severity of the involvement. It is conceivable that the disorder owes its origin to peculiarities in the distribution of the senile tissue process, with selective impairment of certain nervous elements. But it is necessary to explain why these special variations appear only on certain rare occasions, unless one wishes to regard them as purely haphazard phenomena. If they were an integral part of such a common condition as senescence, one would expect to observe their effects more frequently. They point to the presence of some special factor producing an unusual vulnerability of certain nervous structures, a factor which in all probability lies outside the sphere of senescent influences and which gives no evidence of being exogenous in nature.

In the light of the foregoing considerations, grave doubts concerning the existence of genuine senile chorea may be expressed. This is in agreement with the views of Kehrer, Peter and Grünthal on the subject. Kehrer was inclined to believe that senile chorea was really a form of Huntington's chorea in which hereditary tendencies were undetected because of inadequacy of the family history as obtained under ordinary circumstances. In the present case a senile tissue process was associated with a clinical picture suggestive of Huntington's chorea in many ways. It is possible that the senile changes merely precipitated an underlying disorder of the Huntington type. According to this view, so-called senile chorea occurs in families in which the hereditary vulnerability to choreic disturbances has become attenuated. As a result, the patients may

reach a more advanced age and it may be necessary for a more or less full-blown senile process to develop before the less susceptible structures are sufficiently affected to produce a choreic clinical picture. This might explain, in part at least, the difficulty in demonstrating hereditary influences in such cases. Since the observations indicate that chronic chorea can not be attributed to senile changes alone, the hereditary element, even though attenuated, is to be regarded as the decisive factor in its origin.

SUMMARY

A case of chronic and progressive chorea in an elderly adult is reported. Although a definite family history of chorea could not be obtained, many clinical features were suggestive of Huntington's chorea.

Anatomically the striking feature was an abundance of senile plaques in the putamen and caudate nucleus, which also showed diffuse degenerative changes of the small nerve cells. Similar but less marked alterations were observed in the cerebral cortex.

The question whether the case should be classified as one of senile chorea is discussed. It is suggested that this disorder is not genuinely senile in the sense that senescent influences are solely or primarily responsible for its occurrence. Senile chorea may really be a form of Huntington's chorea in which the hereditary vulnerability has become attenuated, with the result that senile tissue changes are required to elicit the choreic disturbance.

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SUBARACHNOID HEMORRHAGE WITHOUT SIGNS OF MENINGEAL IRRITATION

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The problem of subarachnoid hemorrhage has only recently been called to the attention of the medical practitioner. The first case reported in the United States was by Leopold (1) in 1914. Wide recognition of this syndrome by clinicians was delayed until the middle of the last decade. Systematic presentations of this disease in textbooks have all been relatively recent. A number of extensive reviews of this subject have already been reported by Symonds (2), Biernacki and Brack (3), Strauss, Globus and Ginsberg (4) and others. It is worth while to call attention to an unusual clinical finding in this disease—the absence of signs of meningeal irritation with definite bleeding into the subarachnoid space.

It is common experience to find blood in the spinal fluid of patients with head injuries without any evidence of meningeal irritation. Rossi (5) has commented on this fact, though his explanations are not clear and are difficult to accept. Occasionally even purulent meningitis may run its course without meningeal signs especially in infancy (Koplik (6)) and in old age (Urbantschitsch (7), Schlesinger (8)). A man in the seventh decade was seen at the Montefiore Hospital. Otogenous purulent meningitis was found at necropsy. There were no signs of meningeal irritation during life. While unquestionably rare, it is difficult to estimate the frequency of such cases because such patients are usually not tapped.

No one has commented on the clinical importance of the fact that non-traumatic subarachnoid hemorrhage may be present without a stiff neck, Kernig or Brudzinski. While isolated cases are included in the large number of reported cases (Jungmichel (9), Wenderowicz and Sokolansky (10), Kowalew and Schimanski (11), etc.), speculation as to the incidence of this type of case is evidently futile, for until recently, with rare exception, only those cases showing signs of meningeal irritation were punctured. Many cases similar to those included in this report were not investigated from this angle and, therefore, probably remained unrecognized.

Bleeding into the subarachnoid space was found by a number of investigators when a spinal tap was done during routine spinal puncture. Such cases have been reported in general paresis by Targowla (12), and Fontecilla and Wehrhahn (13). Blood was found in the spinal fluid without any signs of meningeal irritation. Hutchison and Baillie (14) found

blood in the spinal fluid of a man who was being prepared for a plastic operation on his nose. A few days later he developed signs of meningeal irritation.

It is important to bear in mind the accepted criteria for bleeding due to trauma by the spinal puncture, as distinguished from spontaneous hemorrhage into the subarachnoid spaces. The reported cases unfortunately often fail to give the spinal fluid findings in detail. True bleeding into the subarachnoid spaces is characterized by its being equally intense in three or four test tubes, by the absence of clotting and the presence of supernatant xanthochromia, unless the bleeding is very recent.

The importance of knowing about subarachnoid bleeding without meningeal irritation is evident. It may throw light on many hitherto obscure neuropsychiatric syndromes, such as transitory confusion, fleeting hemipareses, passing intense cephalalgias, isolated attacks of severe vertigo and problematic stuporous states. Cookran (15) saw a ruptured aneurysm with an old history of recurrent hallucinatory states. It is not widely known that subarachnoid bleeding may cause transitory psychoses, (Baonville, Ley and Titeca (16)). Many of these patients recovered without a spinal tap. One of the patients observed at The Mount Sinai Hospital recovered from a previous meningeal syndrome without a spinal tap. It is well known that the organism can efficiently take care of effused blood in the subarachnoid space (Sprong (17)). The brain of a man who died from some other disease a few weeks after a meningeal hemorrhage, was examined. No gross traces of blood were found anywhere in the intracranial cavity. The fact, therefore, that a case clears up rapidly and completely is no proof that subarachnoid bleeding did not take place. With the experiences recorded here it becomes evident that the clinical concept of subarachnoid hemorrhage must be widened to include cases without signs of meningeal irritation. Seven cases are reported.

CASE REPORTS

Case 1. A forty-four year old Jewish man was admitted on November 28, 1933 to the Montefiore Hospital for the second time. He had been in the hospital from February to May 1931 with arterial hypertension and repeated transitory attacks of auricular tachycardia. He was readmitted because of recurrent attacks of epigastric distress since August 1933. On awakening the day after his admission he could not move the right side of his body. Examination on the same day showed a complete right hemiplegia, a right Babinski and right sided tendon hyperreflexia; there was motor aphasia. He was wide awake, made contact with the examiner and obeyed commands. The blood pressure was 280 systolic and 70 diastolic; the optic discs were edematous with dilated veins and multiple small hemorrhages in the periphery with one larger hemorrhage on the right disc. The spinal fluid was equally bloody in four tubes, did not coagulate and showed supernatant xanthochromia. The blood and the spinal fluid Wassermann tests were negative. He died six days after admission with a terminal bronchopneumonia.

The autopsy showed extensive intracerebral hemorrhage in the left hemisphere with rupture into the subarachnoid space. No meningeal signs were present in spite of extensive bleeding into this cavity. All observers agreed as to the absence of stiff neck, Kernig and Brudzinski signs. The patient was awake and apparently in contact with his environment. It is well known that in deep coma, especially with intraventricular bleeding, no meningeal irritation is present. As the patient regains consciousness, meningeal signs sometimes appear. No stupor or coma was present in this case. If no deep coma is present, cerebro-meningeal bleeding is usually seen with signs of meningeal irritation (Jona (18), Case 4). Kranes (19), Fontecilla and Wehrhahn reported similar cases of intracerebral lesions which ruptured into the subarachnoid spaces without clinical signs of meningeal irritation.

It is becoming increasingly clear with accumulating experience that the presence of persistent aphasia, and marked sensory changes is indicative of an intracerebral focus and that blood over the hemispheres does not usually cause such clinical changes. Deviation of the head and the eyes to the side of the lesion was not present in this case. The changes in the fundi were the only signs pointing to probable intrameningeal bleeding.

The second case presented a somewhat more unusual problem.

Case 2. A 23 year old married woman was admitted in stupor to The Mount Sinai Hospital on September 10, 1934. She had been in stupor about thirteen hours. For three days before she lost consciousness she had complained of some occipital headache and appeared to be depressed. She was urged to go on a vacation. While away, she continued to complain of mild occipital headache. She could not be awakened one morning. She apparently continued to sleep, though she could be aroused sufficiently to be fed for a few minutes. She was seen eleven hours after this stupor was discovered. She appeared to be sleeping. The pulse was 76 to 80 per minute; respirations were eighteen per minute; her skin was dry; she was lying on her back. She resisted passive movements of her eyelids. Her eyeballs did not deviate upward. She could be awakened by shouting. She did respond to simple questions and accepted drinks. When not stimulated vigorously she promptly became somnolent. She was evidently annoyed by pain stimulation.

She did not appear physically ill. The temperature was 100°F. by rectum. Her heart and lungs were normal. There was no acetone or alcoholic odor to her breath. There was no stiff neck, Kernig or Brudzinski; the knee jerks and ankle jerks were equal and active; no change in tonus was found; there were no dyskinesiae; the pupils were somewhat small, about equal in size and completely fixed to light. Accommodation could not be tested. The fundi were normal.

Soon after her admission to The Mount Sinai Hospital she awoke, was well oriented, behaved normally and with complete amnesia for the stuporous period. Her neck was not stiff and no Kernig sign was found. Lumbar puncture immediately following admission showed uniformly bloody fluid with a pressure of 150 mm. of water. The day after her admission she was alert, oriented and showed no signs of meningeal irritation. One observer thought that she had a slight stiff neck—a slight resistance to forward flexion. He, however, admitted that it was not marked enough to make a diagnosis of meningeal irritation without other data. During her further stay in the hospital she complained of occasional mild occipital headaches and pain

in the posterior aspect of the right lower extremity with hypalgesia in L5 to S5. The pupils reacted sluggishly to light on admission but a day later were found to react promptly to light and in accommodation. She continued to improve and on September 24 her spinal fluid was clear. No clear meningeal signs were observed during her entire stay at the hospital.

Ten years before this last admission she was treated in the same hospital for the sudden onset of a meningeal syndrome—stiff neck and Kernig sign following sudden severe headache and vomiting. She had retention of urine for eighteen hours. There was slight bilateral external rectus weakness at the same time. The patient recovered. No spinal tap was done. She was considered an abortive case of encephalitis.

The only sign of organic disease before admission was the pupillary rigidity. This prompted the spinal tap. The diagnosis of her physician was hysteria.

The bloody spinal tap was a surprise to all the attending physicians. They were all tempted to consider the blood as traumatic. The spinal fluid findings were, however, typical of spontaneous bleeding into the subarachnoid spaces.

The history of a previous attack is of great interest. When confronted with a problem of this type it is useful to emphasize the importance of previous transitory nervous or mental syndromes. The occurrence of such episodes is strong evidence in favor of recurrent bleeding from a constant source—perhaps a leaking aneurysm.

The definite meningeal signs during the previous attack indicate the variability of response at different times in the same individual to identical noxious factors.

Complete transitory pupillary rigidity is a relatively rare finding in subarachnoid hemorrhage, though it has been noted by Pugh (20), Dowling (21), Hyland (22), Bosch (23), and others. The more usual pupillary change is that of a changing size and inordinate variability of the response to light. The unilaterally dilated pupil is occasionally seen with massive bleeding over one hemisphere and with oculomotor palsies. Extremely miotic and fixed pupils are characteristic of intraventricular bleeding. This patient's pupils were not at all miotic. Rigid pupils are seen with syphilis.

A much more common problem is the later onset of meningeal signs. This may be due to a rupture of an intracerebral focus into the subarachnoid space. It is more usually not associated with such a complication.

Case 3. A school boy of 14 was admitted to The Mount Sinai Hospital on complaining of severe headache. Two days before admission he complained of severe frontal headache. He was examined by his physician who did not find any evidence of meningeal irritation. He suspected meningitis and repeatedly looked for these signs. No signs of meningeal irritation were found for two days. On the third day stiff neck and Kernig sign appeared and a temperature of 101°F. was noted.

On admission physical examination was negative. The neurological status showed right pupil slightly dilated, bilateral Kernig, stiff neck, drowsiness and some blurring of the left disc. Lumbar puncture showed a uniformly bloody fluid with supernatant xanthochromia. The pressure of the spinal fluid was 290 mm. of water. While in the hospital he developed a left external rectus palsy which had not cleared up entirely when he left the hospital two months after admission.

Case 4. A widow of 36 was admitted with a right hemiplegia of about a half day's duration. The onset was sudden and was preceded by a prodromal period of one week of dizziness. Her blood pressure was 120 systolic and 80 diastolic. The neurological examination showed a complete right hemiplegia with complete motor and partial sensory aphasia. There were marked sensory changes on the entire right side of the body involving all modalities of sensation. Visual field defects were not present. There were no meningeal signs before admission and for a few days after she entered the hospital. The pupillary reactions were normal. A few days after admission some rigidity of the neck and a mild Kernig sign were noted. A lumbar puncture showed 1100 crenated blood cells. Xanthochromia appeared on later punctures.

Cases of this type are much more numerous in the literature than those in which no meningeal signs were noted throughout the course. Ramsay (24) found the meningeal syndrome coming on after one day, Achard (25) after three days, Baillie and Hutchison after five days, and Vogel (26) not till after ten days. In Vogel's case, in spite of the meningeal bleeding being due to the rupture of an intracranial aneurysm, the chief complaint for ten days was backache—no headache.

The next case is interesting because of the presence of psychogenic superimposition in the nature of a conversion hysteria. Without a lumbar puncture the whole clinical picture would have been considered functional, especially since recovery can take place spontaneously.

Case 5. A 38 year old woman with a history of recent serious familial and economic difficulty, suddenly developed a severe headache thirteen days before admission. The headache had continued with only an hour or two of milder pain until the time of admission. The headache, which was generalized, was somewhat more marked in the left occipital region but did not radiate.

On admission, the patient showed generalized tenderness of the skull and weakness; the abdominals were not elicited; the tendon reflexes on the right were somewhat greater than those on the left and she had a complete midline diminution of sensation for all modalities on the left side of the body. There were no meningeal signs. A spinal tap revealed uniformly bloody fluid. The headache was slightly relieved and on the third day following admission another spinal tap still showed definitely xanthochromic fluid but the red blood count was markedly reduced. The patient now felt much improved but eleven days later when she was permitted to leave her bed she again developed headache and a spinal tap again showed extremely bloody fluid. Two subsequent taps were performed and the patient gradually improved. She left the hospital on October 21, 1935.

The absence of meningeal signs during recurrence of the bleeding is worth noting. The functional hemisensory syndrome remained unchanged throughout the period of observation. The conversion hysteria may have preexisted the onset of meningeal bleeding or may have appeared in reaction to this sudden threat to ego integrity.

The last two cases were admitted because of severe headache.

Case 6. A 57 year old man entered the hospital for relief of headache of two weeks' duration. Severe occipital headache appeared in reaction to no evident circumstance. It was not relieved by medication.

The only significant facts in his past history were a discharging left ear thirty years ago with an exacerbation four months before admission and an appendectomy six weeks before under spinal anesthesia.

On admission an examination showed: percussion tenderness over the entire skull; there was a purulent discharge from the left ear, absent abdominal reflexes and a bilateral Babinski sign. The lumbar puncture showed a xanthochromic fluid with 150 red cells, 30 lymphocytes and 10 polymorphonuclear cells. A second tap showed similar findings. At no time during the period of observation were any signs of meningeal irritation noted. Recovery was complete and rapid. Serological studies were negative.

Case 7. A 51 year old tailor was well till he had an upper respiratory infection for three days two weeks before admission. About three days after this respiratory infection cleared up he was overwhelmed by a powerful odor apparently coming from some clothes in his shop. He became nauseated and unsteady. He had to remain at home because of constant severe frontal headache and blurring of vision. He was dizzy and sleepless. When he tried to walk he staggered. On one occasion he vomited. In addition there was numbness of the fingers with shooting pains in the upper extremities. On admission examination showed the pharynx to be injected; there was no fever; he did not appear acutely ill; his blood pressure was 190 systolic and 110 diastolic; the pupils and fundi were normal; there was an unsustained nystagmus on lateral gaze and a left lower facial weakness. Meningeal signs were not present. Lumbar puncture showed xanthochromic fluid, eight white blood cells and a number of crenated red blood cells; the character of the spinal fluid made the diagnosis of subarachnoid hemorrhage quite certain. The blood and spinal fluid Wassermann tests were negative. He recovered in a few weeks.

CONCLUSION

Subarachnoid hemorrhage can take place without signs of meningeal irritation, even in the absence of coma. Seven cases are reported.

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FURTHER STUDIES OF THE SYNDROME OF ECHOLALIA, ECHOPRAXIA, GRASPING AND SUCKING

THE SYNDROME IN THE INVOLUTIONAL PERIOD

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INTRODUCTION

In a previous, more extensive paper (1), the original clinical tetrad of echolalia, echopraxia, grasping and sucking was described in various pathologic neuropsychiatric conditions, as seen in eleven personally observed patients with vascular disease, toxic-infectious states, organic degenerative processes, psychoses, and post-epileptic confusion, including two recovering from insulin hypoglycemia. The literature pertinent to each symptom of the tetrad was reviewed and the significance of the qualitative and quantitative variations of the tetrad was discussed.

The syndrome was found to appear as the result of two main kinds of pathogenesis: (a) in disorders primarily due to interruption of *pathways*, as in cerebral vascular disease; and (b) in conditions due primarily to dysfunction of the total brain integration, as in toxic-infectious states, post-epileptic confusion, etc. These differing quantitative processes provide the opportunity for comparing the correlating qualitative clinical variations.

Those conditions, such as hemorrhage, which interrupt *pathways* or impinge on nuclear masses, leave the personality relatively intact and hence capable of modifying, by tone or grimace, the "echo reflex." In these states there are usually associated pyramidal tract signs, aphasia and occasionally apraxia. The tetrad, in such a case, may be due to thrombosis of the artery of Sylvius (as in the case described by Raymond (2)) in addition to other cortical arteries in the region of the Rolandic and Sylvian fissures, involving the premotor areas which govern the final organization of fine vocal and mouth movements, as well as those of the hand. Hence, since neuroconduction, as such, is not disturbed, the *regression* in these patients is *isolated neurologically* to grasping, sucking, and echolalia of a "reflex" type, echopraxia being interpreted as merely an adjunct language response, as in primitive sign language.

In this study, however, it is proposed to examine a group of cases illustrating only the second kind of pathogenesis; namely, conditions capable of disturbing brain integrative processes *in toto*. As stressed in

the previous paper (1), in these states changes of personality occur which may go on rapidly to visible organic degenerative disease; or, which may rest for many years at a psychotic "level" of disintegration; or, as in post-epileptic confusions may clear up in a few days. If permanent, such regression may be devastating. The echolalia, echopraxia, grasping and sucking in these patients is *not* modified by the deteriorated or psychotic personality. The imitation takes on *significance* and *purpose*, as may even the grasping and sucking movements. Although the patient may be paraphasic and neologistic with jargon tendencies, pyramidal tract signs are usually not present until the deterioration has proceeded for many years. The occurrence of the syndrome in this form, in recovery from insulin hypoglycemic shock, would indicate that it is the qualitative clinical expression of a critically lowered rate of cerebral oxygen utilization, i.e. an expression of diminished cerebral energy exchange.

The involutional period is recognized to be a period of "ebb tide" in the life cycle of the individual, and more strikingly in women. Not only does the sexual apparatus begin to undergo atrophy (negative growth) but, as in growth processes generally, the entire body undergoes manifold and subtle changes which we need not enumerate here. The internist and neuropsychiatrist encounter especially at this period vasomotor-crisis, "dysthroidism" of sympathetic origin, psychoses varying from mild depressions to severe melancholia and dissociated, schizophrenic states, as well as ill-defined "changes in personality" which may be the first harbingers of catastrophic degenerative disease.

In this paper three cases demonstrating the tetrad of echolalia, echopraxia, grasping and sucking will be presented, as it appeared in women in the involutional or post-involutional period observed at Bellevue Psychiatric Hospital. These patients are still alive, two in a State Hospital where they are reported steadily deteriorating, one in the custody of her family. Histopathologic correlations, therefore, are not as yet available.

CASE REPORTS

Case 1. M. H., a female aged 47, was admitted to Bellevue Psychiatric Hospital February 13, 1936 (Case 7 of the previous paper (1)). Her daughter and cousin described her as an exceptionally neat and clean woman who had always been very bright but a little nervous. Her husband had died six months previously, and she had been quite prostrated. She began to show menstrual irregularities, menstruating as often as three times a month. For many years she had had a tremor of both hands and arms, more on the left. She had always had a slight hirsutes of the chin and a bilateral divergent external strabismus. A month previous to admission she became very religious, thought she saw the Virgin Mary in the skies, and began going out into the streets to gather all sorts of rubbish, odds and ends which she called "orders" and which she said had great value for her daughter, C—. The first thing she took was a handkerchief from her daughter's fiancé and to his amazement rubbed her head with it. She then began to go into stores and order all sorts of

things, stopped people on the street and asked for money. She would not pay for any of the things she ordered and would not let her daughter out of her sight. She became exceedingly obstinate and difficult to control, showed marked agitation at being constrained from her acquisitive tendencies and finally was admitted to the Bellevue Psychiatric Hospital.

On admission the patient was oriented but began immediately to pester the doctor for "orders for C—." She showed perseveration and paraphasia of a mild degree. The grasping seemed more of a purposive type than the so-called forced grasping. Once she had hold of any object it was only with great difficulty that she could be persuaded or forced to loosen her grip. She showed bilateral intention tremor more marked on the left, in which extremity pseudo-athetoid movements and adiadochokinesis were also noted. Perseveration became marked. She coined such words as "supermentry orders" and "charter tickets." A key to her was a "key order."

Echolalia. Echolalia was elicited in only one way with any degree of constancy — by using the daughter as an intermediary for the stimulus. When the daughter imitated the examiner, the patient imitated at once. In this way the patient became conditioned to the examiner's stimuli and would repeat what he said. But this echolalia was not automatic.

Echopraxia. Exactly the same relationship held in the imitation of gestures. The moment C — imitated, the patient would imitate. While the patient would repeat anything that C — would do, she would not repeat absurd calculations, in the correction of which she showed remarkable accuracy. She could make relatively difficult calculations with great ease. After a few days she became sufficiently conditioned so that she would occasionally repeat the absurd calculation and then correct it.

Grasping. As noted above, this was more of a purposive type although the patient showed no discrimination in the kind of object to which she clung with such tenacity. Once she fastened on the examiner's ring and it was only with great difficulty that her grasp could be broken. She would not clutch the finger of anyone but her daughter, C—. Otherwise her grasp clung to anything she could carry. Once she said to the examiner: "I will take your whole body home."

Sucking. There were no reflex sucking movements but if an object was held in front of her mouth and her hands restrained she would snap and bite at the object and become extremely agitated when prevented from securing it in any way.

Encephalogram revealed that the lateral ventricles were slightly dilated. Otherwise there were no suggestive findings.

Comment. The writer has not succeeded in finding a parallel case in the literature although snapping and biting movements and grasping-to-hoard activities have been separately described for many years in various types of insanity. The etiology in this case is probably that of an organic process. Transitory hallucinoses occur in such cases, but these seem to be relatively inconstant and to disappear as the more profound organic signs make their appearance. The relation of the psychologic transference and imitation to the daughter which could be conditioned toward the examiner is of great interest in considering the relation of these processes to so-called "psychoanalytic regressions." This problem of transference and imitation on a psychologically selective level comes out strikingly in cases of echolalia and echopraxia as they occur in psychoses, especially in schizophrenia. A

follow-up of this patient reveals that her condition remains as described. She now believes that the State Hospital in which she is confined belongs to her.

Case 2. A. O., admitted to the Bellevue Psychiatric Hospital November 2, 1936, was 45 years of age at the time of her admission. Her medical and neurologic history previous to the onset of the present illness was essentially negative except for the fact that when she was a child her father struck her on the head with a bottle. There was no history of familial disease.

Considering her previous personality, it is important to note that she devoted her life to the care of her father after her mother's early death, an event which had shocked her to prostration. The patient had never had sexual intercourse, and except for a brief engagement just before the menopause, there had been little or no social contact with the opposite sex. Her priest stated her confessions were without much content.

Her sister recorded that the patient's present illness began 4 years previously just after the menopause at which time her hair turned completely gray. She complained of pain in the legs, became restless, refused to eat various foods neglecting fruit juices and other sources of vitamin C. She was apparently afraid to eat for two years previous to admission. Her sister stated that her hands had recently begun to "clot up."

Two months before admission, her father died. Following this she became confused, garrulous, alternately laughing and crying, and complained of pain in her right thigh and leg. She imagined she saw lights.

She was admitted on October 15, 1936 to the Medical Ward of Bellevue Hospital, where she was described as "psycho-neurotic" with infectious arthritis. A few purpuric areas over the right leg and left hand were noted and the predominant blood findings were enumerated as hemorrhagic diathesis, moderate anemia, and thrombocytopenia. In addition she was thought to be "Parkinsonian with hyper-tonia and hyperkinesis." A diminution of cevitic acid in the blood and on excretion test was found. This was thought responsible for the "hemorrhagic diathesis" and "peripheral neuritis." However, high vitamin diet did not alleviate the symptoms and the patient's mental state became progressively worse. It was observed that she became increasingly depressed and reacted strongly to suggestion. There was a slight unexplained rise in temperature. She was finally transferred to the disturbed ward of the Psychiatric Hospital. Neurologic examination there revealed no evidence of neural involvement. The vitamin deficiency though present was not considered etiologic, but secondary. X-ray examination of the skull was negative.

Mentally the patient was agitated, restless, and confused. She prayed constantly. At times she screamed: "I promise to be faithful and loyal." Her speech had a marked religious content. She said to the examiner: "Are you Joseph -you are Christ and I want to see my father—Oh Christ save my soul I have to confess something. I want to live."

She became markedly paraphasic, but with peculiar reference to all the examiner's objects as hers or as belonging to a member of her family.

(Key?)—"Key to my best cellar. I am in it. The key to my sister's house."

(Watch-chain?)—"That's the watch-chain that my father has."

(Comb?)—"That is my comb."

(Money?)—"That is money I might have had."

At this stage she was noted to have bilateral grasping and sucking reflexes with marked "mimicry." Her gait became broad-based. She showed marked echo-

praxia using both hands when the examiner used one. She had many echolalia responses. Speech remained disorganized in paraphasic directions, thus:

(Puddle?)—"I don't recall."

(Puddle?)—"Person—woman on feet."

(Puddle?)—"Water. It will last forever."

(Puddle?)—"Puddle. Puzzle. I don't know."

(Envelope?)—"Something inside a letter."

(Frustrated?)—"Something taken from a fig."

(Watch?)—"Time—watch—blind and instantaneous."

The patient continued to be confused, restless, agitated, markedly echopractic, showing disorganization of speech with bilateral grasping and sucking. She made erotic advances to the examiner. She was finally committed to a State Hospital.

Comment. At the outset, the vitamin deficiency can be dismissed as secondary to the fear of eating which began during the menopause. High vitamin diet (both B and C) did not alleviate the condition.¹

The previous personality while not psychotic showed an infantile relationship to the father. At the menopause there is a definite "change in personality" which becomes accentuated and accelerated apparently by the shock of her father's death. The regression continues until there is a complete disorganization of significant relationships. Language concepts deteriorate. At this phase bilateral grasping, sucking and marked echopraxia manifest themselves. The fragmentary nature of the echolalia responses is associated with the complete disorganization of speech. It is significant that objects not hers, which she can *name*, are interpreted as belonging either to herself or to her sister. This characteristic it will be remembered is also found in case 1 in relation to the patient's daughter.

Case 3. V. A., a female, aged 45, a former professional dancer, was admitted to Bellevue Psychiatric Hospital on May 13, 1937. She had been married for 3 years. She was apparently well up to two or three weeks before admission except for the fact that two months previously she had become preoccupied with some freckles on her face and had them removed chemically (with salicylic acid) by a beautician. As a result, the skin of the neck was burned so severely that she bumped her head thrashing around in bed, becoming quiet only after narcotics were administered. Since the treatment she complained of "low vitality." She had been known to go on alcoholic sprees. Her menopause had begun several months previous to admission.

She had lived in New York City for eighteen years until about a month before admission when her husband took her to California by auto. She wrote home about the "scary" roads but apparently was not otherwise apprehensive. She had never before been superstitious or concerned much with religion. She had, however, smoked to great excess, consuming four to five packages of cigarettes a day, and frequently used barbiturates for insomnia. She had a history also of taking aspirin and coca-cola in large quantities.

After two weeks in California she began to act in a peculiar fashion. She was very fearful when crossing the street. Her husband observed her standing in the

¹ This patient has been studied and presented by Dr. D. A. Shaskan, at a Bellevue Psychiatric Conference with especial reference to the possible etiologic relationship to vitamin deficiency.

bathroom washing the bowl aimlessly with a brush. She became increasingly frightened and the husband returned with her to New York. He said: "She didn't always talk sense. We'd see some cows and she'd say 'There's some moo-moo's.' She just sat and rode and wouldn't talk. She'd eat ice-cream or milk, that's all. She would move her bowels in the car and in bed. She plays with herself in bed, won't talk, nor feed, nor dress herself."

On admission the patient sat trembling and grimacing. She was mute. Occasionally she blurted out her name to persistent questioning. She appeared toxic and tremulous, was tense and resisted physical examination, with a rather pained, agonized expression on her face. Physical examination was essentially negative. Neurologically the positive findings were fragmentary echolalia and perseveration, with some palilalia, marked sucking and bilateral grasping. The left pupil was dilated and larger than the right. There were no pathologic reflexes. She was incontinent. She remained confused. She lay in bed picking her nose and masturbating. No echopraxia was noted. There was a marked aphasia.

Her responses were as follows:

(Where are you?)—"Where am I at."—"Anna"—"Anna."

(What is the trouble?)—"What is the trouble?"—"Don't know."

She remained in this state for almost three weeks when gradually speech began to return. She moved around continuously making little attempt to rise from the horizontal plane. She fumbled around aimlessly with her right hand. She began to respond to questions but somewhat irrelevantly. When asked why she sucked objects, she said: "On general principles."

The left pupil remained larger than the right. Her reaction to pain was of the "thalamic" variety with a mimetic right lower facial palsy. The tendon reflexes were equal and lively. She continued to show speech abnormalities. Shown a key she called it a "glay." She repeated questions thus:

(What day is today?)—"What day is today."

(Ever take opiates?)—"Opiates."

She was irritable at times and when tested for sucking with the examiner's key said: "Don't tease me with *my* keys," thus also showing pathologic possessiveness.

She then began to confabulate and was frequently facetious. Encephalogram a week after admission showed: "A small amount of air in the ventricular system, which does not appear to be dilated, the anterior horns are vaguely visualized; the right is apparently normal. The outer pole of the left appears to be depressed with no apparent deviation from the mid-line. Cerebral sulci on right are demonstrable; sulci on left are very vague. Findings suggest arachnoiditis on left side." Ventriculography later revealed air only in the subarachnoid spaces. Ventricles were not outlined.

About six weeks following admission the patient's speech improved to the point where she was able to answer questions much more relevantly. Sucking persisted to the day of discharge. She became more active, moved around and got out of bed. She still had a dull and somewhat bewildered attitude. Six weeks after admission she was discharged in the custody of her husband to go to a private health resort.

Comment. While in this case there are some data which suggest possible toxins such as salicylic acid, there was no evidence of reducing substances in the urine at the height of the regressive process. Neither the alcohol nor the barbiturates were used in sufficient quantities to produce a toxic psychosis. There was, however, evidence of changes relative to the menopause, namely "low vitality," increasing tension as evidenced by

the very excessive smoking. She had married late in life and when separated from her home and family, her general apprehension began. It is interesting to note that the regression goes deep enough to involve the selection of foods. She would eat only ice-cream and milk. The neurological signs, such as dilated pupil, and lively reflexes, can be attributed to the arachnoiditis as evidenced by the encephalogram.

The exclusion of a toxic etiology leaves only the fact that here also an individual at the menopause suddenly underwent a severe regression with mutism, echolalia, marked grasping and sucking. Echopraxia is commonly absent when the patient is confused.

DISCUSSION

Three patients, all women, are presented as cases showing various degrees of personality deterioration in the involutional or post-involutional period. In each case the grasping, sucking, echolalia, echopraxia varies qualitatively and quantitatively. In the first case, the syndrome appears only in a transference relation to the patient's daughter. The grasping and biting are purposive and acquisitive in character. In this patient neologisms are present and the condition remains constant with gradual deterioration. The syndrome appears six months after the menopause. In the second case, the grasping and sucking approach more closely the classical organic type, the echolalia is fragmentary, the echopraxia being very marked. In this case the syndrome appears several years after the menopause, although nervous symptoms were present immediately following the onset of involution. The vitamin deficiency is looked on as secondary to the fear of eating, although there is a possibility that such a vitamin deficiency might produce a selective cerebral irreversible change which might then not yield to vitamin therapy. This seems unlikely in view of the fact that the vitamin deficiency was never very great so far as could be determined. There was never any evidence of neuritic changes. In the third case, the regression is much more acute and profound with a rather marked amelioration of symptoms but not with complete recovery; degenerative processes may begin acutely. The presence of a dilated pupil is ascribed to an arachnoiditis alone. Arachnoiditis frequently appears in degenerative disease. From the point of view, therefore, of the qualitative evaluation of symptoms and the neurological analysis the one feature in common in all these cases is the appearance of the degenerative disease in the involutional or post-involutional period. The fact that these appear with different time intervals in relation to the beginning of involution and with different courses is to be ascribed to individual differences in constitution. If one looks upon degenerative disease as due to an inherent defect in the fertilized ovum, then it is to be expected that degenerative processes will occur at various periods in the life cycle when the organism undergoes diminution in somatic energy. The involutional and post-involutional period is such an epoch.

From the point of view of personality and the environmental factors which might be especially severe at this period, there is the fact that in each case some emotional shock is present. In the first case, the death of the husband; in the second case, the death of the father; in the third case, the separation from home and family. The coincidence of emotional shock and the involution may be of etiologic importance.

Cases such as the ones presented demonstrate the need for a coherent psychobiologic theory. Deterioration has to be evaluated not only from the standpoint of the natural differences in constitution, but also as to the physiologic effect of anxiety. The personality has to be looked upon as an integrative process in growth and decay. It is hence necessary to know the relationship of body, brain, and environment, not only at any given time, but also in the relation of one such period to an earlier one. At the involutional period the organism has, so to speak, to come to accounts for the anxieties of a lifetime. Any period in life when growth energy is on the wane may be more critical.

These cases show not only the developmental relationship of primitive imitation in speech and gesture to primitive movements like grasping and sucking, but also demonstrate the fact that movements like grasping and sucking cannot be attributed, in the disorganized personality, to a lesion of any single portion of the brain. The experimental removal of the premotor area and its connections may release grasping, as may also an isolated tumor in the human, as in the cases of corpus callosum tumor reported by Cramer (3). However, isolated lesions do not produce such personality changes; consequently when grasping and sucking together with automatic imitation occur in cases of severe personality regression, one must look upon this tetrad as indicative of disorder of the brain integrative function which expresses itself in disordered function in hand and mouth activity. From the standpoint of cerebral energy exchange, in the case of the isolated lesion, the brain's energy exchange is normal, only the *pathway* is disturbed. In the severe personality regression, brain integration is abnormal while the pathway is intact. Various quantitative disturbances in brain energy exchange will result in various qualitative clinical differences. It is hence quite futile to attempt to localize grasping and sucking, echolalia, and echopraxia in such disease entities.

Finally, as to a possible relation of these cases to known degenerative disease, it will be remembered that Pick (4) studied echolalia intensely; he regarded it as a primitive speech learning phenomenon due to disease of the temporal lobe. Echolalia in proved degenerative disease has been reported by many writers, (see especially Liepmann's case report (5) which showed atrophy of the entire brain, more marked in the dominant hemisphere and especially in the frontotemporal region, areas normally supplied by the artery of Sylvius). Goldstein (6) believed that echolalia was a form of "transcortical aphasia" critically produced by a lesion of the motor out-flow area. Whether these cases represent degenerative

diseases allied to Pick's disease or whether they are indicative of a special form of degeneration is as yet impossible to state.

SUMMARY

1. Three cases of personality regression demonstrating various relationships of the tetrad of echolalia, echopraxia, grasping and sucking are presented.

2. The regression is considered as related to constitutional changes in cerebral energy quanta in the involutional or post-involutional period.

3. Some of the differences between isolated neurologic regression and disturbances in total brain integration are discussed. It is considered that the symptoms of the tetrad in this latter form cannot be localized since they indicate disturbances in total brain integration.

4. The need for a coherent psychobiologic theory is stressed.

5. The possible relationship of these cases to Pick's disease is mentioned.

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THE EFFECT OF ERGOTAMINE TARTRATE ON BODY TEMPERATURES

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During the course of investigations of the migrainous syndrome, it was noted that patients commonly experienced coldness of the extremities during the attack. This observation was associated with the well known theory that the migrainous seizure is an expression of local constriction of the blood vessels due to disordered activity of the vegetative nervous system (1). Recently, Wolff (2) has contradicted this theory by demonstrating that there is *dilatation*, and not *constriction*, of the temporal artery during the migrainous seizure. Presumably, the striking clinical benefit frequently obtained by the use of ergotamine tartrate is through its effect on this disturbed vasomotor control (3). The exact mechanism of this drug's pharmacological action in ameliorating migrainous attacks is still subject to controversy. There is strong evidence produced by Wolff's studies to indicate that ergotamine causes constriction of the dilated cerebral arteries, thereby relieving the headache. According to Röthlin, (4) ergotamine paralyzes both the motor and inhibitory endings of the sympathetic nervous system. On the other hand, the relief of pruritus, sometimes obtained by the administration of this drug, would favor the hypothesis that the sensory nerve endings are also affected (5).

Pool and Nason (6) declare that the injection of ergotamine in the cat constricts the arteries of the dura and the skin, while there is no consistent effect on the arteries of the pia.

Lennox (7) demonstrated that, in man, the injection of ergotamine increased the blood flow through the brain.

Kottmann (8) has stressed the attempt to group migrainous subjects into two types: vagotonic and sympathicotonic. This classification is stimulated by the assumption that ergotamine is only therapeutically helpful to the sympathicotonic type.

The rise in blood pressure following injection of ergotamine, with frequent elevation of internal and external body temperature, might provoke

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Ergotamine tartrate (Gynergen) was supplied through the courtesy of Sandoz Chemical Works, Inc.

a suspicion that this action is thyrotropic. However, this view is militated against by the slowing in pulse rate which invariably occurs, associated with a lowering in metabolic activity. Marine (9) discovered that a striking fall in heat production in normal rabbits was obtained by the injection of ergotamine tartrate subcutaneously. He concluded that

TABLE A

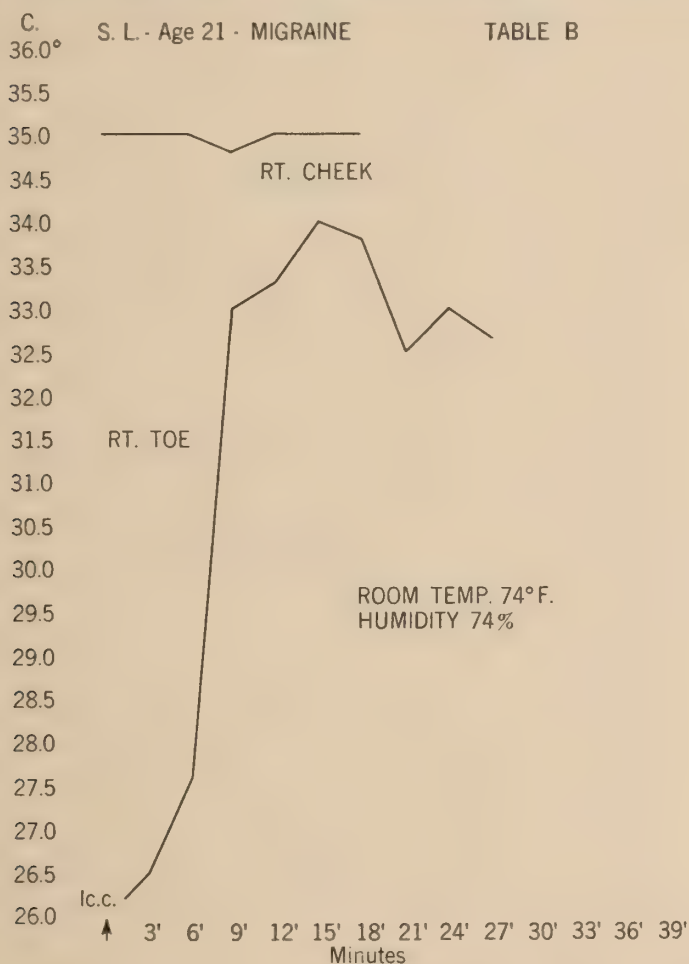
REGION	MIGRAINE	EPILEPSY	CONTROL
CHEEKS	RRR no change	R	R
	RRR R→F	F	R
	RRR		R
	RR		R & F
THUMBS	RRR	F & R	R
	FFFF	F	R
	RRRR		no change
	no change		R
	no change		
TOES	FFF	R	
	RR	R→F	R
	F & R F→R		R
	F & R		F→R
	RRRRRR		F→R
RECTAL	RRRRRRRR	R	R
	FF	R	R
	(2 subjects not recorded)		R
			R

R = rise, F = fall, F→R = fall then rise.

ergotamine was a powerful sympathetic depressant because the injection of ergotamine also caused a lowering of metabolism in thyroidectomized rabbits. A similar drop in body temperature was noted in rats and dogs after the injection of ergotamine, according to Rigler and Silberstein (10).

It was decided to study the reaction of body temperatures to the sub-

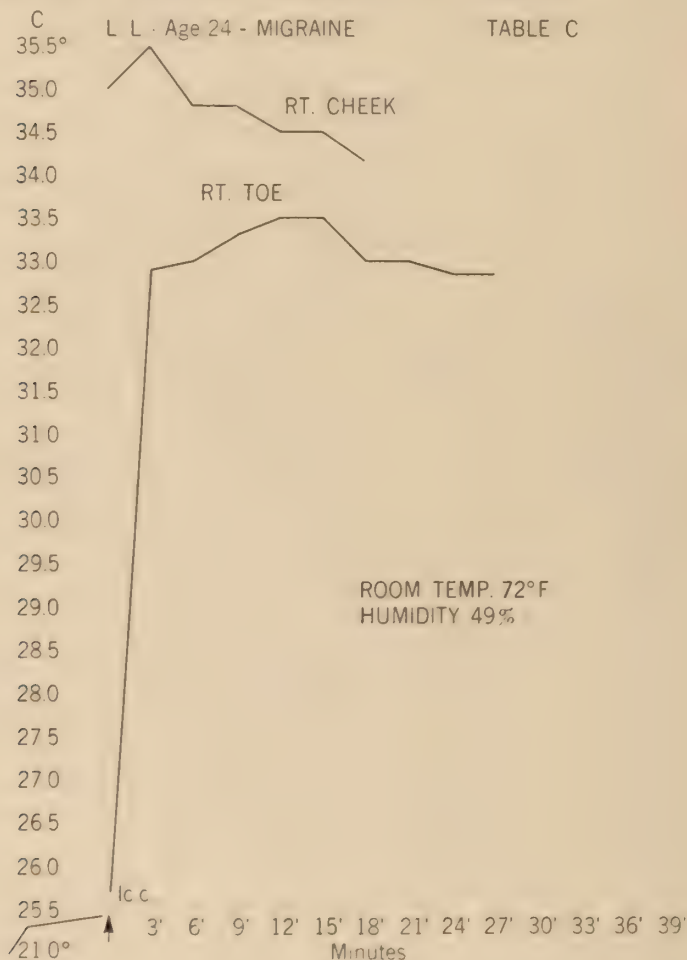
cutaneous administration of ergotamine tartrate in human subjects. Thirteen migrainous subjects, two epileptic subjects and four controls were observed. Both the skin temperatures and the rectal temperatures were noted. The apparatus used consisted of a thermocouple for recording the skin surface temperature and an electrical resistance thermometer for



periodic measurement of the rectal temperature. Inasmuch as the temperature of the skin surface of the toe has been shown to fluctuate more than any other surface area of the body, determinations were made at three minute intervals in this region (11). One cubic centimeter of the solution of ergotamine tartrate (1 to 2000) was given in the arm. The discomforts sometimes attending the administration of the drug have been

described elsewhere. None of the subjects had a severe headache before the test was made.

The results have been tabulated as shown in Tables A to D.



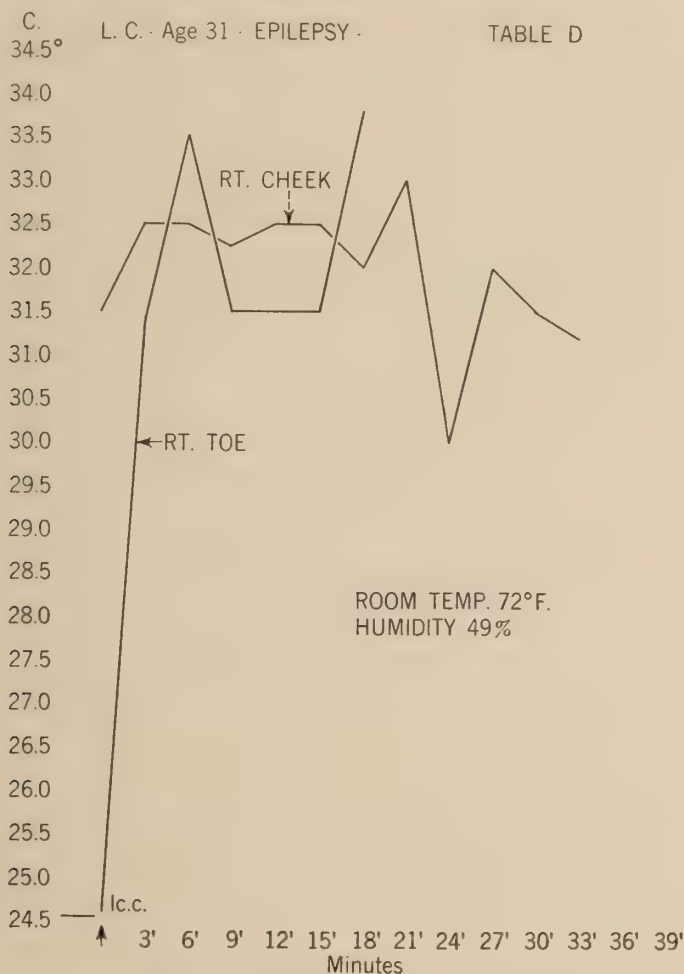
SUMMARY

This preliminary report of the effect produced by the injection of ergot-amine tartrate on body temperature shows:—

1. Tendency to a rise in surface skin temperature over the cheeks with flushing of the facies frequently noted.
2. Marked tendency to a rise in rectal temperature.
3. Variability in reaction over the toes and thumbs; some showed a rise, some an immediate fall, while others displayed an oscillatory alteration.

There is sometimes a striking difference between the right and left sides of the body.

4. Patients suffering from such paroxysmal disorders as epilepsy or migraine, seem to react with greater intensity to the effect of ergotamine tartrate. This may be linked to the common observation in clinical neu-



rology that such patients present evidence of marked vasomotor instability.

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SOCIAL DIAGNOSIS: A METHOD SUGGESTED FOR THE INVESTIGATION OF SOCIAL PROBLEMS

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Society's first concern is survival. It therefore develops its institutions in response to economic and cultural traditions and needs, and tends to disregard the reaction of the individual. In so doing, it may carry with it the germs of its own destruction. It is only after the elemental needs of the community have been satisfied and the group settles back to enjoy the fruits of its efforts, that it may, for the first time, become aware of the unrest upon which it is founded. Here will be found to lie the elements that have not been taken into account and which are bent on achieving greater recognition, even destroying the civilization if necessary. The community then begins to ask itself, "What is wrong with us?" The sociologist will answer by pointing out certain political, social and economic trends which have succeeded in dispossessing the individual and depriving him of his security, both economic and libidinal. The psychiatrist, however, can make this information more specific by showing how the individual reacts to the social structure. It is interesting to note that communities are attempting to understand the temper of the individual and the psychologic reasons for his behavior, and to substitute love and understanding for force. The basic unrest may thus constitute a sufficiently vital reason for inducing the group to change the content of its code of laws.

The coming of age of the group also has a definite bearing upon the individual. As the social pressure upon him becomes less urgent, he can begin to think in terms of himself as a person. He no longer needs to lose himself in the common purpose and can now begin to look to his own welfare. Have his sacrifices brought him the security and happiness he hoped for, or has he been exploited by the more powerful members of the group, who have arrogated most of the privileges to themselves? Has he enough freedom of libidinal expression or does he feel the restrictions of society as an unwarranted imposition? His observations on these points will help to determine his attitude toward the group. If he finds it to his advantage he may decide to subordinate his selfish interests to the common good; if not, he may insist upon a change.

Other factors also come up for consideration. If the central authority is weak, it may permit the emergence of violent types of aggression, such

as revolution and bloodshed. On the other hand, if it is strong and positive, it will tend to inspire a feeling of security in its subjects. In either case, dissatisfaction may take the form of political changes, radical agitation, delinquency, general disregard for law, loss of initiative, racial prejudice and sexual indulgence. Which form it takes will depend upon the social and cultural background of the body of the people. Some of these are permissible activities as far as the group is concerned, others are not, depending upon whether they tend to undermine the foundations upon which the group is built. The important thing to remember, however, is that although the social structure depends upon social, economic, cultural and political factors, the effect of the social structure upon the individual can best be expressed in psychologic terms, since the external experiences of the individual are as a matter of course translated into the common denominator of psychologic experience. In the matter of racial prejudice, for instance, one may say that it is a universal phenomenon, being based on the fact that people are apt to distrust those who are unlike themselves. Its appearance in certain milieux, however, must be explained not by its universal nature, but by what functions it serves in that particular situation at that particular moment. The social significance of racial prejudice is therefore best determined by its effect upon the individual: how much it means to him and how it helps him solve the problem of his insecurity. Since the stability of the group depends upon the reactions of its subjects, it is essential for the sociologist interested in modifying and correcting social forms to keep his finger on the psychological pulse of the people so that he may be aware of what they are thinking.

Before any corrective plans can be made, society must first learn what the disruptive forces are. As Kardiner (1) points out, the individual in his quest for security needs to find expression for his sexual and aggressive tendencies. In doing so he may run up against certain restrictions imposed upon him by society. If the group is insecure it may attempt to crush the protest and abolish any expression of it, or it may disregard it altogether. On the other hand, if it is secure it will try to offer compromises, without, however, allowing its own existence to be endangered. Frequently the insistent knocking on the portals of social consciousness by malcontents produces an uneasiness in the minds of the authorities, particularly if they are aware of their own responsibility in exploiting their subjects. How the individual reacts will depend to a large extent upon what these restrictions are and what compensatory reactions are allowed by the group, as well as upon his own personality and cultural background. Average people will attempt to work out their 'problems along the lines permitted them by society and convention. Instances of such permissible activities are common business practices, social intercourse between the sexes, political changes, etc. The abnormal individual, however, will inject his own personal difficulties into the situation and

react in a rather unconventional manner. It ought to be possible to distinguish between the actions of the individual which are the result of his peculiar pattern and those which are his normal reactions to the group problem. In general, one may say that the reaction of the group is unreliable as an index of the normality of the individual's behavior, since the group mind is inclined to hold on to tradition and to view any deviation as a source of danger. Consequently, it will usually attempt to suppress any efforts aimed at correction. Normal behavior can very often best be determined by a study of a number of individuals who act in accord, since persons living in a certain environment present a uniformity of behavior which is necessary if they are to be accepted by the others. As Alexander (2) states, attention must be paid to those common features in the environment which are characteristic for the community; these, as a rule, will be recognized as historically determined and traditionally transmitted attitudes. In such a study the community is interested not in the individual as such, but rather in the fate of society. The aim is not to correct individual behavior (which is the psychiatrist's function), but to modify the social form. If psychologic insight into the meaning of social institutions is sought, it is only for the purpose of clarifying our thinking and making it more precise. It is important to keep this distinction in mind if we are to avoid being side-tracked. It follows that we are concerned with the typical reactions of the group and not with the atypical or aberrant reactions of a few persons. It is the typical or general reaction which points the way to the basic social pattern; the occasional and highly individual reaction is very often a neurotic response to a situation that may exist only in the subject's mind. To the sociologist such aberrant behavior is meaningless and ineffective, unless the person is sufficiently dynamic and powerful to win followers and sway the forces of society.

Social diagnosis is designed to show society the causes of discontent and the forces which tend to disrupt it. In social diagnosis it is essential to know not only what the physical environment is, but also the significance of each factor in the environment, how it came to develop into the thing that it now is and how the constituent members of the group react to it. It must also learn what the community *mores* mean to the individual, how they fulfill his needs and satisfy his aspirations, what opportunities they offer for advancement and what basic needs in the community they satisfy.

To discover what the physical environment consists of one must know where to inquire for statistical data. In a superficial way, one may also learn what institutions mean to various people by the questionnaire method. Such studies, however, although valuable in themselves, are useless to one who desires to obtain a profound knowledge of the group. It is as if one were to study anatomy in minute detail without any knowledge of function; one is apt to lose oneself in a mass of irrelevant detail

for the meagre satisfaction of having been thorough. Such a procedure is too diffuse for one thing, and does not focus attention on the sore spots. It is clear that a more intimate acquaintance with the individual would give us a better understanding of the situation. This implies a two-fold approach, the sociologic and psychologic. Dollard (3) has utilized this method by combining the usual sociologic studies of society in a southern town with a modified psychoanalytic study of a number of individuals. He has thus succeeded in observing closely how the social form impinges upon the individual. Social diagnosis can be applied to any aspect of the social structure, but it will naturally be used most often to determine the ailments of society. We are interested here in pathologic physiology, as it were, rather than in normal physiology.

To illustrate the above remarks, I might refer to a recent play, "Mulatto," in which is presented the situation of a white plantation owner in the South who has a number of children by his negro housekeeper, and who, according to the custom of the South, refuses to acknowledge them as his own. The children who remain at home are content to accept this inferior rôle. One, however, who has attended school in the North, returns and rebels against the necessity of surrendering his independence. In the ensuing struggle he is naturally destroyed.

According to Dollard, the average negro in the South, as a matter of self-preservation, has accepted the rôle which the white man has assigned to him and in return for his unquestioning acceptance is allowed a certain amount of liberty, namely, the privilege of going about his business unmolested, partial freedom from the restraints of conventionality and the good-natured protection of the powerful white man. If this is not sufficient to satisfy him he is entitled to leave, but rebellion is not to be thought of. Any sign of insubordination calls forth immediate and summary efforts to crush it. It is obvious that the threat to the white man is too great. Even legitimate success in the negro is frowned upon. The white man's defensive uneasiness is a reflection of the constant fear of counter-aggression under which he lives. The development of this need to dominate the negro can be traced to basic economic factors, having their sources in the peculiar environment of the South from the beginnings of slavery. The present subservience of the negro psychologically also is directly related to his slave status. Dollard interprets the negro's submissive rôle as deference to a harsh father whom one must placate openly, but against whom latent hostility is stored. The strength of the father, however, makes for security in the subject. In the play, most of the man's children seem to be aware of these trends and take the easier course by complying with custom. The unruly son, on the other hand, acts out his neurotic pattern in real life. Had he been influential enough to lead an effective mass uprising of negroes, his achievement would have been of great significance sociologically, while his personal reactions

would have been of secondary importance. As it turned out, he was merely a misguided rebel. This illustrates how psychological factors might determine sociological events.

In my capacity as psychiatric consultant to the Family Society of a certain community, I was impressed by the existence there of a rather unusual situation, namely, the prevalence of sexual license, especially incest, and delinquency. The association of the two appeared to be more than casual and suggested an attempt to investigate the relationship between them. In seeking a plan of procedure for such an investigation it occurred to me that Dollard's method could be adapted, with the modification of using social case work records in the place of psychiatric interviews. One who is familiar with case work knows how informing the reports of an alert social worker can be, and how much of the client's personality is therein revealed. Actually, it is found that this plan offers distinct possibilities.

It is difficult for a person who has become accustomed to a certain environment to be able to judge it objectively. Just as the primary sense organs of the body tend to lose their sensitivity to a continuous stimulus, so the individual fails to see the unusual about him after he has lived with it for some time. The new-comer, however, can readily point out what to him is striking in the situation. The first step in a plan of procedure then is to determine what the outstanding features in the community are; these can serve to direct attention to the sore spots in the cultural set-up. They may consist of a variety of factors, such as poverty, unemployment, alcoholism, immorality, delinquency, mental disease, intellectual backwardness, ill-health, etc. Such problems can be taken up and used as the starting point for our investigations, just as in studying the neurotic's personality we start off with his presenting symptoms. A series of individuals representing all shades of opinion may be interviewed to determine the personal value to each of them of the particular phenomenon in question. In addition, it is necessary to trace back the phenomenon historically to learn how it came to develop to its present status and to correlate it with the cultural and economic background of the community. Such a study should give us a fairly complete picture of the significance of the culture and the behavior of its members.

The following case and discussion are presented in summary in order to indicate what direction such studies might take. A complete investigation would necessarily include a number of similar cases, from which conclusions could then be drawn.

A father, taking advantage of his parental authority, induced his two daughters to have sexual relations with him. There was some reluctance on the part of the girls and one of them contrived to get out of the situation by marrying the first man available. Her subsequent marital life was very unhappy and her personality underwent considerable deterioration.

She neglected her home and children, went on drinking parties, had a number of extramarital relationships and wasted her money. The other daughter openly rebelled against her father and as a result was driven from the home. She went to live with her sister, of whose behavior she disapproved, and attempted to correct the management of the latter's home. This continued for several months until her boy-friend, irked by her father's insistence that he marry her, left her entirely. She became very resentful at the injustice of events and broke loose from all restraint, becoming promiscuous and practising prostitution openly. This type of rebellious activity finally eased up and she returned to her own home after obtaining employment.

The following problems will naturally come up for consideration in the analysis of any situation like the foregoing:

PSYCHOLOGICAL

1. What is the significance of incest to the individuals who practise it and those who are close to the situation? What is their reaction to it?
2. What are the mental mechanisms behind their behavior? What happens to the individual's superego and his sense of guilt in such a situation?
3. What new problems of adjustment does it bring up?
4. Why do people living in the same environment react differently?
5. How does the aggressor react to the group and authority? Does he cling to it or does he break away entirely? If he clings to it how does he rationalize his behavior? What determines his desire to cling to the group? How does he react to society's rejection? How does it affect his inner life, and immediate relationships?

SOCIOLOGICAL

1. What is the social, cultural and economic setting which permits a man in a civilized community to let down the barriers against incest? What factors favor its occurrence?
2. What is the relationship between incest and moral degradation, occurrence of delinquency, prostitution and marital unhappiness?
3. What do the church, court and organized society have to say about incest, and how do they attempt to reestablish the standards of self-respect and acceptance of responsibility?
4. What is the wider influence of incest on the community? Does it tend to disorganize the social life?
5. What are the criteria of social acceptance?

To answer these questions case records may be sufficient. It may be necessary, however, to make special note of the opinions and observations of others, as well as to record incidents that may be pertinent. In addi-

tion, historical and traditional sources will have to be tapped in order to obtain a rounded out picture of the situation. It will be seen that sociology is concerned with the social and legal aspects of the problem, the genesis, development, causes, effects and treatment of the phenomenon. Psychiatry, on the other hand, is interested in mental mechanisms and in learning why people act the way they do. Each, of course, is complementary to the other.

Although the primary purpose of such a study is to understand social phenomena, a no less important result of the study as far as psychiatry is concerned, is the determination of how much the social situation is responsible for the individual's response and how much of the difficulty of adjustment is due to his own personality? In other words, is reality too demanding for the average person and to what extent will direct treatment of such an individual be successful if he continues to live in this environment? The answer to this question may determine the validity of much of our present therapeutic efforts in psychiatry, and may indicate the importance of treating society as an adjunct in the reduction of mental illness.

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SOME NOTES ON REPRESSION AND ON EGO INTEGRITY IN ORGANIC DISEASE

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The purpose of this communication is to present case material illustrating the following limited aspects of psychosomatic interrelations: — (1) that organic brain disease may damage the function of repression and cause the patient to experience anxiety by the release of previously controlled intrapsychic problems which have then to be handled in various other ways, and (2) that organic disease of any type may act as a threat to ego integrity and so liberate anxiety against which some psychic defence must be erected. The anxiety in such cases arises essentially from the threat to the security of the individual.

I

Organic brain disease is, in a sense, a partial dissolution of the ego, both structurally and functionally. This partial dissolution of the ego, by its interference with the ability to repress, liberates anxiety because it permits the emergence of repressed strivings into consciousness.

These emergent strivings can be handled in various ways. The individual may give direct expression to these impulses without anxiety. This type of behavior is especially well known in post-encephalitic children, and requires no further elucidation here.

In some instances the damage to the brain will permit a certain release of the inhibited impulses, though, perhaps due to the integrity of some of the ego functions, a neurotic compromise still remains possible. This type of adjustment is at a relatively higher level since the patient eventually inhibits the impulse, though at the expense of suffering from distressing compromise formations, i.e., neurotic symptoms. The following case of post-encephalitic psychoneurosis is capable of being understood in this way and is a good example of this type of problem. The patient, during the acute stage of encephalitis, first carried out his inhibited impulses; as he recovered, he inhibited them again but suffered from neurotic symptoms.

Case 1. The patient, a 40 year old man, was married to an aggressive and abusive woman. He was a mild, meek individual who had apparently adjusted himself to his wife's abuse and aggression and inhibited any hostile feelings he might have felt towards her. He had occasional neurotic symptoms, but on the whole was well adjusted to the situation. During the mild influenza epidemic of November, 1936

he became ill, though he tried to work in spite of his illness. One day he got as far as the subway station but had to return home. His memory of what happened after that is clouded. He came into the house, smashed the furniture, threw things at his wife, shouted at her for her continual mistreatment of him, and violently aired all his grievances about her. After this period of excitement he became very drowsy and stuporous, and was admitted to the hospital in that state. Neurological examination showed fleeting, scattered and changing signs:—nystagmus, pupillary signs and slight difference in reflexes. His course in the hospital was uneventful. He recounted his long and unhappy married life, and pointed with some pleasure to the fact that he had finally asserted himself. However, before discharge he had again reconciled himself to the previous state of affairs. He was followed in the outpatient department; there he complained of an entirely new set of numerous and disabling symptoms; various aches and pains, paresthesiae and sensations of discomfort all over his body. He had never suffered from these complaints before. The overt status at home continued to be the same.

Aggressive impulses may be released and handled in a manner less adapted to reality than conversion symptoms are. The aggressive impulses may be turned against oneself. The following case may be interpreted as demonstrating the simultaneous release of aggressive and self-destructive trends.

Case 2. An 8 year old boy was admitted because of restlessness of one week's duration. There was mild fever, tachycardia, red throat, enlarged cervical lymph glands and generalized purposeless movements, definitely choreic in pattern. A diagnosis of chorea was made. His behavior varied:—his predominant attitude was sullenness and resentment against the environment. He refused to answer questions and closed his eyes when spoken to. Sometimes he would assume a posture resembling the fetal intrauterine position. He would claw at his bedsheets and showed active resentment to anyone who approached. He had to be held down because of his extreme motor restlessness and violence. At times he would throw himself about, crawl under the bed and repeatedly strike his head against any hard object. He was frequently heard to mumble threats of suicide. When questioned explicitly, he always affirmed this desire to kill himself and said he would as soon as he had a chance.

The next two cases illustrate suicidal attempts upon occasions when there was organic-functional impairment of brain function, by alcohol in one case and by epilepsy in the other. In the first case, after a series of contributory and precipitating factors, the patient became depressed. The suicidal impulse only appeared after the patient drank in order to cheer himself up. The point brought out here is merely that the suicidal impulse became conscious and overtly active while the patient was drunk.

Case 3. A white male, 24 years of age, had been a sporadic drinker since the age of 16; when drunk he would become irritable and look for a fight. In the past five years he had had frequent quarrels with his mother and sister, leading eventually to his leaving home. A week previously, his fiancée jilted him. He became depressed and blue, but not suicidal. On the day of the suicidal attempt a friend offered to cheer him up by going out to drink with him. When he returned home that night, somewhat drunk, without much reflection, he swallowed a box of luminal

tablets. He was found unconscious. The next day examination showed a slight difference in reflexes, otherwise the neurological status was negative. Although still slightly drowsy, he was clear, friendly and cooperative. In the next two days the depressed mood lifted. He laughed, felt foolish about his suicidal attempt, and was interested in returning to work as soon as possible. There were no self-accusatory trends.

In the next case there is no conscious material relating to overt aggressive impulses. We are presented with the picture of a markedly frustrated boy in whom thoughts of suicide were more or less strongly present over a period of many years; the suicidal impulse was carried into action during a period of cerebral functional impairment due to an epileptic seizure.

*Case 4.*¹ The patient, a 29 year old male, had been having epileptic seizures since the age of 10. The seizures would come in series of attacks lasting several days, then leave him free for several weeks. The aura was usually a peculiar feeling or a clouded state which would last about twenty-four hours. After several days of repeated seizures there would be a post-convulsive period of confusion which lasted about a day. There would be amnesia for the entire period of several days. He had been unable to work, go to school or engage in any of the normal social activities of a young man of his age. He was entirely dependent upon his mother and siblings. In reaction to this situation of total frustration and helplessness there was a strong feeling that life wasn't worth while, and that he would be better off dead. However, he was careful to state that even though life wasn't worth living he would never voluntarily take his own life. In the past five years he had made three suicidal attempts, two of them during the auras and one during a period of post-convulsive confusion. He had no memory for these episodes. He was found twice with the gas turned on and once with a rope tied around his neck.

II

The threat to ego integrity which an illness or defect inherently contains is a potent source of anxiety, and requires strenuous defence. Schilder (1) has discussed this problem in terms of health as a psychic experience. Patients utilize protean modes of defence against such anxiety. These defences may be fragmentary psychic constructions, just as much of a screen against the anxiety as is necessary, or they may be profound changes in thinking, affect or level of adjustment. The defences may be successful or unsuccessful.

Partial defences against certain intellectual inadequacies will be mentioned briefly. The structure of these defences is relatively simple.

Case 5. An old female showed all the organic changes associated with senility. There was nocturnal restlessness and a mild degree of confusion during the day. She could answer simple questions correctly and promptly. Such questions had to contain no more than a single thought or idea, such as her name or age or birthplace. If any degree of complexity were introduced she at once cupped her hand to her ear

¹ From the Out-Patient Department of the Neurological Service of Dr. Israel Strauss, The Mount Sinai Hospital.

and said, "What's that? My hearing isn't good, you know." When questions were again put very simply she again answered without any hesitation and with no attempt to resort to the defence of hearing difficulty.

Another patient developed a much more elaborate defence against her own inadequacy. The defence assumed the shape of a farcical pseudo-delusional system, partaking of the nature of confabulations.

Case 6.² This patient was a middle-aged female with all the clinical and serological signs of paresis. There was marked euphoria and dilapidation of personality. She had much difficulty with test phrases. When given phrases to repeat she stumbled at once and gave the rejoinder, "That's English, I can't speak English." When asked what language she could speak she said she could speak Pidú. She offered to translate from English into Pidú, and was given the word 'good-morning'. She promptly replied, "Hel-lo," and said with a satisfied smirk that that was in Pidú. When given other words she always gave some English synonym in a halting and stilted fashion. As time went on, and as her speech became more dysarthric she became a multi-linguist. She could speak French, Russian, Belgian, Bulgarian, etc., but she never admitted she could speak English. Her manoeuvres were always the same:—she spoke in halting, stilted synonyms, and always in English.

In these last two cases the problems requiring defence were simple problems and were met by simple defences, which were successful. This type of pseudo-delusional formation can be separated from delusions going out of previously existing intrapsychic problems.

If we turn from these simplest to the most severe problems we may see patients who are suddenly faced with an immediate and terrible threat to life. The threat is so severe and so imminent that the individual may be unable to rally any defence mechanism whatever, and the fear of death breaks through in unalloyed fashion.

Case 7. A middle aged woman was admitted for medical observation. On the ward she was suddenly taken with acute upper abdominal pain and terrific anxiety. The intense fear and panic were the outstanding features. She was so fearful that she was unable to describe her complaints or even ask for help. There was a look of stark terror in her eyes. She died in twenty-four hours. Post mortem examination showed that death was caused by coronary occlusion.

In this patient the threat to life was so immediate and overwhelming that there was no opportunity to erect any defense against the fear of death, and it was present in its baldest and most agonizing form.

On the other hand, certain long-lasting illnesses in which there is no immediate threat to life may permit the individual to erect not only certain intellectual constructions which act as denials, but also the elaboration of affective states which effectively color all experience and make all reality falsely pleasant. Multiple sclerosis is perhaps the outstanding example of such a condition; patients with slowly developing brain tumors or

² From the Psychopathic Hospital, State University of Iowa, Iowa City, Iowa.

paresis behave similarly. In these patients there is a successful defence against the anxiety.

Case 8. This patient, a middle aged male, showed the usual signs of multiple sclerosis, optic atrophy, spastic ataxia, incoordination, disseminated neurological findings. He was cheerful, friendly and garrulous. This facade of fatuous cheerfulness was almost, but not quite, constant. He would on rare occasions have spells of depression and tearfulness, or at times would be irritable and angry. When in his usual mental state he never admitted he was sick. When asked how long he had been sick he would carefully correct the examiner and restate, "You mean how long I have a little trouble in walking." He would then proceed to explain how a new pair of shoes made him stumble, and so lose his job on the railroad. He was quite disabled for work.

The euphoria of patients with diffuse disease is probably greatly supported by their lack of insight. It is quite understandable that patients with sensory aphasia should find it easier to develop euphoria (Schilder); their anxiety is less because they are less capable intellectually of appreciating their defects.

Patients in toxic-exhaustive deliria may successfully deny their illness and deficiencies.

Case 9. A 57 year old negro fell four stories and suffered multiple fractures of three of his extremities. One leg was amputated at the thigh because of infection. He had repeated blood transfusions; he developed a mild bronchopneumonia and a confused delirious reaction. He was febrile, exhausted and toxic. He became over-talkative and incoherent. Although he was in a large plaster spica, and was immovable in bed unless moved by attendants, he constantly asked for his clothes and wanted to leave and go to work. There was complete absence of any anxiety about his illness. "Why should I worry?" He would not admit that he was helpless in bed. He was not depressed; he discussed his job casually; he was not worried about his inability to care for himself. When his attention was called to his amputation he said he would get a wooden leg and walk all right.

In contrast to either the stark fear of death or its successful opposite, the complete denial, there are other methods of meeting the anxiety: projection may be utilized. The next case may be analyzed in the following way: first there was a marked overt fear of death, partially handled by projection to the outside; the projection became successful with the attachment of the idea of death to her husband; at this stage there was no anxiety though she suffered grief at the imagined death of her husband. As the patient failed, the defences disorganized and the anxiety reappeared before death.

Case 10. A young negress was severely ill with chronic glomerulonephritis and bronchopneumonia. There was edema of the face and the typical twitchings often seen in uremia. The urinary and blood findings were those of uremia secondary to this kidney disease. She developed a delirious state and a high state of excitement. She refused to permit the nurses to come near her, was in a violent panic, and had vivid visual hallucinations. She would shriek out, "I don't want to die. I don't

want to die. I'm going to die." The theme was constantly repeated with a great deal of terror. When asked about her hallucinations she said, "There's a man coming. He's over there. He's got a knife. There he is. He's going to kill me." Concerning the nurses, "They know I'm going to die. They won't let me live. They won't let me live. They don't help me." Two days later the patient lost her anxiety and panic, but she was wailing with grief; she had no fear of dying. She sobbed and moaned, "My husband is dead. I know he's dead. It come to me. Oh my husband is dead." No amount of reassurance could quiet her. Two days later she was stuporous and more confused, spoke thickly, admitted her husband was alive; the overt fear of death was again present. She died in coma three days later.

The projection was at first only partly successful. With the hallucinations and paranoid attitude there was much conscious panic. Later when the idea of death was projected into another person there was no anxiety but a marked display of grief. As coma and death approached, the projections disintegrated and the conscious fear of death reappeared.

The anxiety may be handled in a simple and yet very drastic way, by complete withdrawal from reality.

Case 11. A 12 year old boy had a two weeks' history of migrating polyarthritis. On admission a diagnosis of acute rheumatic fever was made. During the first five weeks the boy presented nothing unusual. He then developed signs pointing to pericardial effusion. He suddenly refused to eat or talk. He would not void or move his bowels. He lay motionless in bed, and only the alertness of his eyes indicated that he was aware of what was going on about him. There was nothing to point to clouding or confusion. Neurological examination was normal. There was a frightened apprehensive look about him. There was no waxy flexibility. Repeated attempts to induce him to talk or to explain his fears were of no avail. He had to be tube fed. After awhile he began to give fragmentary responses to questions and began to eat. After two months his improvement had progressed to the point where he would walk about the ward, feed himself, perform errands for the nurses and doctors and give partial and hesitating answers to questions. He was given an intravenous injection of sodium amytal with good transient effect. He became cheerful, laughed, showed no fear. Among his productions on various occasions were, "I was afraid I would die. . . . They were going to cut my legs off. . . . I didn't want to come to the hospital. . . . They want to hurt me. . . . They take (dead) people away on stretchers. . . . They want to put me in the side room. . . . That man wants to hurt me. . . . I'm afraid."

Examination of the boy's productions revealed that he had not simply withdrawn from a situation correctly appreciated, but that he had projected his fears concerning his bodily integrity in various directions. His anxiety was projected into almost all of reality, and in his attempt to seek safety he withdrew from everybody and everything.

SUMMARY

Organic affections of the brain may interfere with repression and liberate strivings previously repressed. These strivings may then be directly expressed, or compromise neurotic symptom formations may be effected

to inhibit direct expression of these impulses. The impulses may be deflected against oneself, leading to suicidal trends. Suicidal impulses may be brought to the surface or into action.

An organic illness or defect may operate as a threat to ego integrity, liberating anxiety and the need for defence against this anxiety. Partial intellectual constructions may suffice for certain intellectual inadequacies; pseudo-delusional formations may be created. The threat to life may be acute and overwhelming, leading to overt panic, there being failure of erection of psychic defences. On the other hand, chronic diseases may permit the elaboration of affective states of euphoria which successfully color all experience. The successful affective defence of chronic patients is contrasted with the unsuccessful defence in acute overwhelming disease. The tendency toward total affective reactions without insight in patients with diffuse brain disease is noted. Inadequacy or illness may be handled by projecting the fear of death; there may even be complete withdrawal from all real or fancied sources of this fear.

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INTRACEREBRAL EPIDERMOID TUMORS—A CHARACTERISTIC ENCEPHALOGRAPHIC FINDING

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Refinements in indirect methods of diagnosis have enabled the surgeon and neurologist not only to easily localize brain tumors, but also in great measure to predict the nature of them. While the neurosurgeon is still frequently embarrassed at the operating table by totally unexpected findings, the encephalographic-pathological correlations derived from thousands of cases have built up a number of well defined syndromes. Therefore, it seems justifiable to put on record several cases which presented in each instance a bizarre encephalographic picture and which at operation were found to be intracerebral epidermoid tumors (cholesteatomata). It is not unwarranted to believe that this may be a characteristic encephalographic finding.

In passing it is of some interest to note that, in 186 instances of this tumor reported in the literature, in only four cases was the diagnosis made correctly before operation. In addition, practically all of the reports dealt with diploic, suprasellar, cerebellar, cerebello-pontile and fourth ventricle tumors. Only a few cases within the hemispheres have been placed on record and, so far as can be found, the nature of the tumor in these cases was not suspected before operation.

CASE REPORTS

Case 1. History. The patient, a thirty-eight year old woman, was admitted on the first occasion to the service of Dr. Israel Strauss in The Mount Sinai Hospital in November 1930. Six months before admission she noted the slow onset of numbness and coldness of the right leg, which, in the course of five months, involved the right arm. Slight weakness, clumsiness and awkwardness of the right extremities were gradually noticed. There had been no headaches, convulsions or mental difficulties. Her past history was essentially negative.

Examination. The fundi were normal. There was a slight right hemiparesis, a mild impairment of all modalities of sensation over the right side of the body, right dysstereognosis and a right homonymous hemianopsia. There were no defects in language understanding or expression. The general physical examination was negative except for a mild hypertension, the pressures ranging from 170 systolic and 90 diastolic to 140 systolic and 90 diastolic. The intraspinal pressure was 90 mm. of water.

Course. The final discharge note stated that because of the lack of progression under observation and the absence of symptoms of increased intracranial pressure,

encephalography should be deferred. The lesion was considered to be vascular and was localized to the region of the posterior limb of the left internal capsule.

Readmission. The patient was readmitted to the hospital in December 1936 with the same complaints. Her reason for returning was that she had "bad feet." The neurological examination yielded exactly the same findings as on the previous admission, with the addition, however, of a left Babinski sign. There had been no headaches in the interim, no speech or mental difficulties. The blood pressure, however was 220 systolic and 100 diastolic, and on another occasion 190 systolic and 100 diastolic. In a careful review of her case the slow onset of her symptoms five years before raised the suspicion of brain tumor and and, in spite of the unchanged complaints and the systemic evidences of vascular disease, encephalography was decided upon and performed.

The plates are reproduced in Figure 1. The large honey-comb-like collections of air which seem to occupy the interstices of a tumor baffled interpretation. The ventricular system was displaced to the right and the right ventricle was dilated. All that one could say was that there was a large tumor of bizarre character occupy-

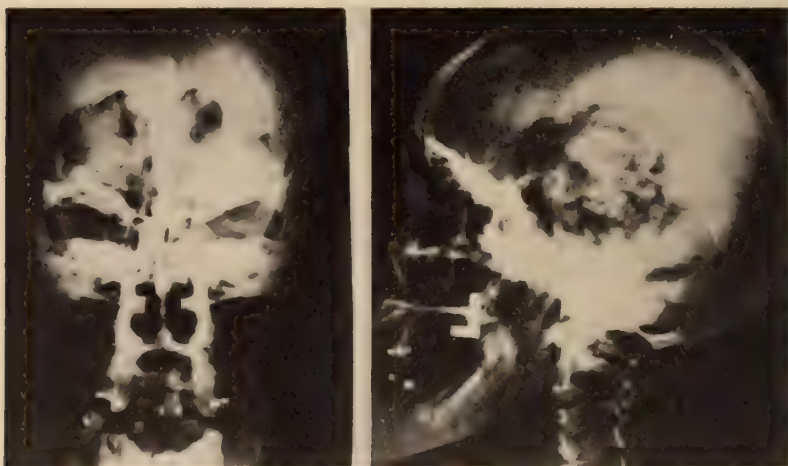


FIG. 1. Anteroposterior and right lateral views show clearly the spongeliike mass of air occupying and displacing the ventricle. The largest amount of air appears on the periphery of the tumor, although there is an illusion of air within it.

ing and displacing the medial and posterior portions of the left lateral ventricle. Operation was suggested to the patient, but was refused, since her symptoms were not distressing and she wished treatment only for her sore feet. The patient was discharged.

The nature of the tumor remained quite puzzling since there was not another tumor in the entire collection at The Mount Sinai Hospital that resembled it. The plates were taken to Dr. Cornelius Dyke of the New York Neurological Institute for an opinion. He had in his collection only one case which in all essential details corresponded to Case 1. The same reticular mass of air occupying and displacing the lateral ventricle was observed in his case. It had proved on operation to be an epidermoid tumor. On the basis of this case he ventured the opinion that the plates of Case 1 represented an epidermoid tumor.

At a departmental conference in which this case was presented as a probable

epidermoid tumor. Dr. Sidney W. Gross remarked upon his experience with a similar case showing the same odd picture. His case, too, at operation had been found to be an epidermoid tumor. He has kindly allowed me to publish his case (Case 2).

Case 2. History. A male, thirty-nine years old, was admitted to the service of Dr. E. D. Friedman at the Beth Israel Hospital for the first time in April, 1934. He complained of inability to speak and of convulsions of one week's duration. The past history was negative. One week before admission the patient's right arm began to jerk uncontrollably. This stopped, but recurred several hours later, and again disappeared after a few minutes. These fits were followed the next night by a generalized convulsion lasting thirty minutes. There was a second generalized convulsion on the succeeding night. During the next two days the patient had frequent convulsions involving the right side of the face without loss of consciousness. These were accompanied by the beginning of difficulties with speech, which progressed to complete motor aphasia within the next three days. He could comprehend what was said to him and was able to wash and dress himself.

Examination. He was able to make sounds but not words, but was able to write his name and use common objects. No pathological reflexes were elicited. A focal convulsion was witnessed, which started with twitching of the right corner of the mouth and spread to involve the entire right side of the body. There was a right central facial weakness and the tongue deviated to the right. The right extremities were slightly weak.

Course. The staff concurred in the diagnosis of a focal lesion in the left frontal lobe and proposed encephalography, but at this point the patient's symptoms began to rapidly clear up. In a few days all signs and symptoms had completely disappeared, and, inasmuch as the findings were meager and the symptoms were gone, he was discharged as a brain tumor suspect.

Readmission. He remained entirely well for two years but was readmitted in June, 1936 in status epilepticus. Two weeks previously he had begun to complain of dull frontal headaches. The day before admission there had been twitchings of the right side of the face and these passed into generalized convulsions. The convulsions were controlled with intravenous sedatives. Examination showed a stuporous male who could be prodded into feeble response. The retinal veins were distended. There was a slight right lower facial weakness. The right patellar jerk was more active than the left. There were no pathological reflexes. The spinal fluid was under normal pressure. Flat plates of the skull were negative and encephalography was then performed. The X-ray report stated that there was a mass containing irregular collections of air, which indented the anterior segment of the left lateral ventricle (Fig. 2).

Craniotomy was performed by Dr. Sidney Gross and his operative note read as follows: "A left frontal bone flap was reflected. The cortex appeared normal, but with the brain cannula definite resistance was encountered in the frontal lobe at the depth of 1.5 cm. Aspiration yielded a milky, flaky material. A transverse incision was made into the cortex and a tumor encountered. The capsule was incised and the contents were removed with the curette. The material on the inside of the tumor was wax-like. It was entirely excavated and a cavity the size of a tangerine remained. The capsule was teased out and it was evident that it connected with the ventricle. The wound was closed with a rubber drain left in the cavity."

The patient made an uneventful recovery and left the hospital on the fifteenth day with only a residual slight speech defect. The microscopic report stated that the tissue consisted of hornifying squamous epithelium and detritus containing cho-

lesterol crystals. The section of the cyst wall showed a multiple layered epithelium with a fibrous external layer. The diagnosis was epidermoid tumor with cholesteatomatous changes.

The encephalographic picture was puzzling, but at the time no particular significance was attached to it in so far as suspecting the pathological nature of the tumor. It is of particular interest to note the surgeon's remark: "... it was evident that the tumor connected with the ventricle." The importance of this observation will be discussed later. Although the tumor was large, the ventricular system was only slightly shifted and the tumor appeared as a spongelike mass of irregular collections of air. It is obvious that the encephalographic pictures of Cases 1 and 2 are similar in all essential details. The curious filigree lacework of communicating channels of air is not duplicated in any other type of tumor of which I am aware. Although Case 1 was not verified, one feels almost certain that it must represent an epidermoid tumor, particularly in view of Case 2 and the other verified case alluded to. This presumption is bulwarked by the extreme chronicity of the course which is characteristic of these tumors.

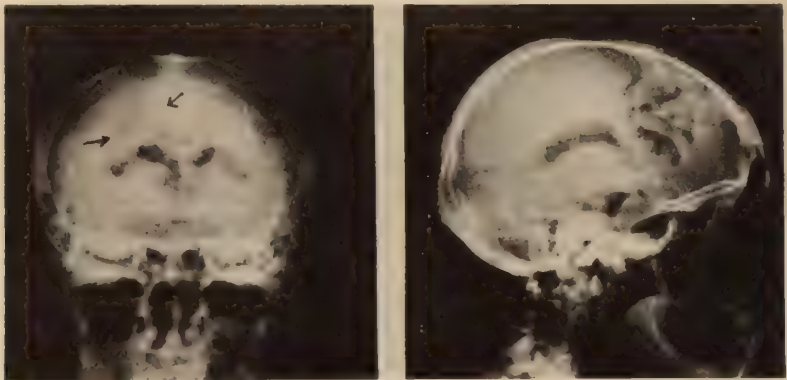


FIG. 2. Postero-anterior and left lateral views show tumor occupying the anterior segment of the left ventricle with the illusion of air within the tumor. The tumor appears lateral to, and above, the left anterior horn.

COMMENT

While the nature and origin of these tumors were for many years uncertain and many conflicting opinions were held concerning them, in recent years the ideas of various workers have crystallized into a uniform point of view that is generally accepted. They are regarded as epithelial fragments that have been dislocated in the course of the formation of the brain and have come to lie within the cranial cavity. Like inverted sacs of skin they grow in size by the casting off of squames into the interior of the sac (Bailey (1)). Indeed, their walls are composed of several layers which mimic in structure and are, in fact, analogues of the layers of the epidermis. The outer layer, stratum durum, however, is fibrous and appears to be an investment from the pia. The interior of the sac is filled by a cheesy substance representing disintegrated squames intermixed with cholesterin crystals formed during the chemical breakdown.

If glands or hair follicles happen to be included in the original aberrant fetal inclusion, the tumor is then spoken of as dermoid, since dermal structures are present. While they are obviously congenital tumors their growth is slow (Craig and Kernohan (2)). They gradually indent and displace the brain and their presence is announced to the patient only when they affect one or more of the cranial nerves or important pathways. Generalized symptoms of intracranial pressure or papilledema are exceptional events in the history of these growths.

So far as this paper is concerned, several interesting speculations arise. How do the epidermoids become intraventricular or intra-hemispheric? How does air find its way into them during encephalography? And, finally, what is the explanation of the curious reticular configuration of the air seen on the films?

The occurrence of epidermoid tumors within the hemispheres and within the ventricles can only be explained by reference to the development of the brain in relation to the skull and meninges. One theory which seems to explain the facts was advanced by Von Remak (3) and Bostroem (4), who considered that epithelial tissue was pinched off by the folding neural tube or split away from the main sheet of epiderm by the developing and interposing flat bones of the skull to take up position within the cranium. Globus (5), in his recent studies on the meningiomas and the development of the meninges, presented arguments in the same direction, though explaining the mechanism somewhat differently. He pointed out that in the formation of the brain coverings, the epidermis and the primary mesenchymal meninx were contiguous and that the laws of chance allow the possibility of fragments of epiderm to accidentally break away, become enmeshed in the primordial meninx and thus be carried far into the cranial cavity in the further development of the pia-arachnoid. By this means epithelial tissue lodged in the interstices of the leptomeninges may be transported, theoretically, to any part of the brain.

This attractive explanation finds confirmation in the observations of several writers who have noted that epidermoid tumors are connected to the pia at some point or appear to arise from it. Critchley and Ferguson (6) state: "Most epidermoids arise from the subarachnoid cisterns. In some instances the epidermoid seems to arise from the apex of the invagination of the pia-arachnoid which forms the velum interpositum and pushes forward the posterior portion of the third ventricle." Again they state: "In the cases of tumors lying within the hemispheres it is under favorable circumstances possible to demonstrate a more or less delicate connection between the growth and the leptomeninges at the base." Munroe (7), noted in a case of a parietal lobe epidermoid, that "—at one point the cyst wall was connected with the pia and the falx." Nehrkorn (8) observed, in an epidermoid tumor buried in the depths of the temporo-occipital lobe, that it was connected with the basal meninges in

one place. Berka (9) describes an intramedullary spinal cord epidermoid whose capsule was—"in relation to the pia-mater in the posterior fissure."

These comments by different authors are significant in establishing the conception that the meninges bear a direct and important relation to both the occurrence and location of epidermoid tumors. It seems definite that these tumors are always connected to the pia-arachnoid in some way. Further evidence is found in the fact that the outside coat of these tumors, from which they derive their pearly luster, is not ectodermal at all, but mesodermal. One cannot escape the inference that this fibrous layer, the stratum durum, is derived from the pia which originally ensheathed the epithelial inclusion.

Since the primary meninx not only goes to form the meninges and dural septa but also takes part in the formation of the choroid plexuses and tela choroidea, one can see the explanation of the occurrence of intraventricular epidermoids. According to the generally accepted belief, the cerebral hemispheres in ballooning out from the primary vesicles enfold and surround the pial projections carrying the vessels destined to become the choroid plexus. Though this pia becomes closed within the ventricles, it obviously has the same origin as the pia elsewhere, and the law of probability allows that a fetal epithelial inclusion may be lodged in this portion that provides the stroma of the choroid plexus. In this way the occurrence of intraventricular epidermoids is accounted for and the significance of the fact that in reported instances the tumor was connected to the wall of the ventricle is explained. If it were specifically looked for, a pial band connecting the tumor should be found in every case; it should serve as the pedicle carrying the blood supply to the investing tunic.

The epidermoid having started to grow may either push its way into the ventricular wall and slowly imbed itself in the hemisphere or it may grow within and extend through the ventricular system. Stone and Phillips (10) report a case of a dermoid tumor which filled the right temporal horn and extended into the lateral and posterior horns almost completely filling them. The authors state that it was invested with a capsule of connective tissue and attached to the wall of the temporal horn. Love (11) reports an egg-sized epidermoid tumor within the temporal horn which was attached to the medial wall. Mahoney (12) also reports an epidermoid within the ventricle. Only a few such cases have been reported so that it appears as if intraventricular or intracerebral epidermoids connecting with the ventricle are rare. Although in Love's case there was an encephalogram, he made no mention whether or not there was anything peculiar about the air shadow.

In the two cases here reported and the third case alluded to, this curious spongelike collection of air on the films was striking. In each case the tumor appeared to be partly inside and partly outside the ventricle. The explanation of the curious conformation of the air within the tumor is

puzzling for the air apparently is inside. Cushing (13) remarks, apropos of his discussion of these tumors within the fourth ventricle, several of which he reported, that occasionally these tumors rupture into the ventricle producing a sterile meningitis, fever and exacerbation of symptoms for a few days. Perhaps such a perforation, putting the interior of the tumor in communication with the ventricle, sets the stage, so to speak, for the admission of air. In this case, however, the inside of the tumor should most certainly contain cerebrospinal fluid. Since this has never been noted in any of these tumors operated upon, one is forced to conclude that the appearance of air within the tumor is an illusion and that the air actually surrounds the mass. That these tumors are very irregular in out-

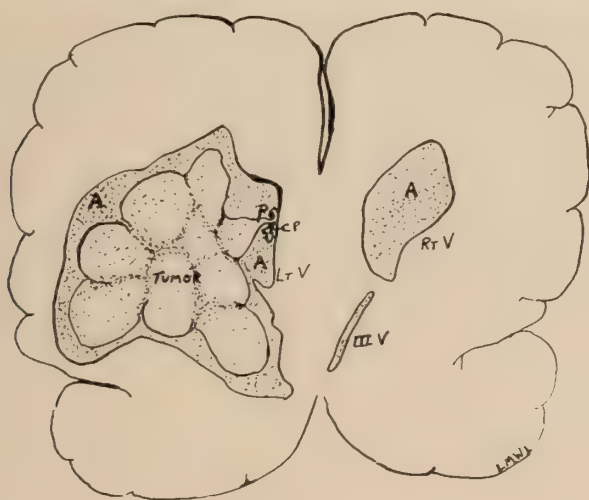


FIG. 3. Diagrammatic explanation of case 1, which portrays the anatomical situation that must exist in order to produce the unusual pneumograms. The ventricular wall is distorted and pushed out by the slowly growing tumor as it imbeds itself in the brain. A, air; C P, choroid plexus; P, pial band

line is well known. It is probable that when air enters the ventricle it passes up alongside the tumor, forces its way into the interstices between the brain substance and the tumor wall and fills the grooves of the surface of the tumor. A study of the reproductions of the encephalograms seems to bear this out. It will be noted that the central part of the mass contains relatively slight amounts of air with the largest channels of air at the periphery.

Figure 3 demonstrates this situation diagrammatically. The odd filigree pattern must merely represent air filling the devious irregular grooves and sulci on the surface of the tumor, as well as the spaces between the tumor and the brain substance.

So far as I have been able to discover, there have not been published any

encephalographic studies of an epidermoid tumor. It would be unwise to declare that this peculiar aerographic picture should be expected in all epidermoids arising within the ventricle. It seems allowable, however, to assume the converse—that is, whenever this configuration does occur, it is most likely due to an epidermoid tumor springing from within the ventricle. As a matter of fact, it seems not improbable that the same picture should be produced by an intrahemispheric epidermoid tumor communicating by a pial band with the subarachnoid space over the convexity. The same mechanical relationships should hold in that case.

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EPENDYMOMAS ARISING FROM THE VENTRICULAR LINING AND CHOROID PLEXUS

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The choroid plexuses in man are little more than folds of the ependymal lining covering a core of highly vascular connective tissue projecting into the several ventricular compartments. The ependymal cells covering the plexuses and those serving as the ventricular lining have a common origin from the cells of the ependymal zone of the primitive medullary canal. In embryos, the neural tube is thinned in certain places to form an epithelial membrane which acts as a roof for the primitive ventricles. At the end of the second fetal month, this ependymal epithelium proliferates and with a covering of vascular pia mater, the tela choroidea, on its outer surface, folds into the fourth ventricle. The choroid plexuses of the third and lateral ventricles are similarly formed. However, even before the ependymal lining has been modified to form the mantle of the choroid plexus, it tends to assume an alveolar or papillary pattern.

It would seem proper to consider together all tumors of ependymal origin, whether derived from a primitive ependymal cell or from the ependyma in a later phase of its histogenesis. This is in conformity with the views recently expressed by Kernohan and Fletcher-Kernohan (1) who nevertheless classified the ependymomas into four groups because of variation in cellular organization. In the first, named by them "cellular ependymomas," the tumor cells appear in masses without any definite pattern or organization. In the second group their so-called "epithelial ependymomas," the cells assume what the authors consider an epithelial formation. The third group is composed of the "myxomatous ependymomas," in which the tumor tissue assumes a definite papillary structure, the core of which has undergone myxomatous degeneration and can be successfully stained for mucin. The fourth group is represented by so-called "papillomas of the choroid plexus." Here the cells reduplicate the villous structure of the choroid plexus and contain mucin both intracellularly and in the core of the papillae.

This classification is fully justified by the material presented by the authors. There are, however, many ependymomas which present mild transitions from one form to another, so thoroughly obliterating the more obvious differences between the types mentioned that it would be more desirable to designate them only by the generic term of *ependymoma*. In the six cases herein presented, the cell arrangements varied from dense

masses with no particular pattern through alveolar and papillary configuration such as to reproduce finally the structure of the choroid plexus. They serve as a good illustration of the close relationship between the various types and their probable common origin.

CASE REPORTS

Case 1. History (Adm. 304398). A 20 year old male was admitted to the hospital on March 7, 1929. Four and a half months previously he had begun to suffer from headaches centering about the vertex. These,



FIG. 1 (Case 1). Gross appearance of the tumor in coronal sections

at first intermittent, later became more continuous and severe. There were also episodes of blurred vision and diplopia, accompanied by vomiting. Tremor of the hands had developed and the patient showed increased irritability.

Examination. There was a bilateral high-grade papilledema. A slight right facial weakness was more apparent on emotional innervation. A Parkinsonian tremor was present in both hands, more marked in the right. The right lower limb was slightly rigid and tremulous. The deep reflexes obtained on the right side were more active than those on the left.

Course. The diagnosis of neoplasm was more favored than that of encephalitis in spite of the Parkinsonian rigidity and tremors. A ventriculography was performed but only an incompletely filled and irregularly dilated right lateral ventricle was visualized. Following the air study the patient appeared to improve and was allowed to return home. His head-

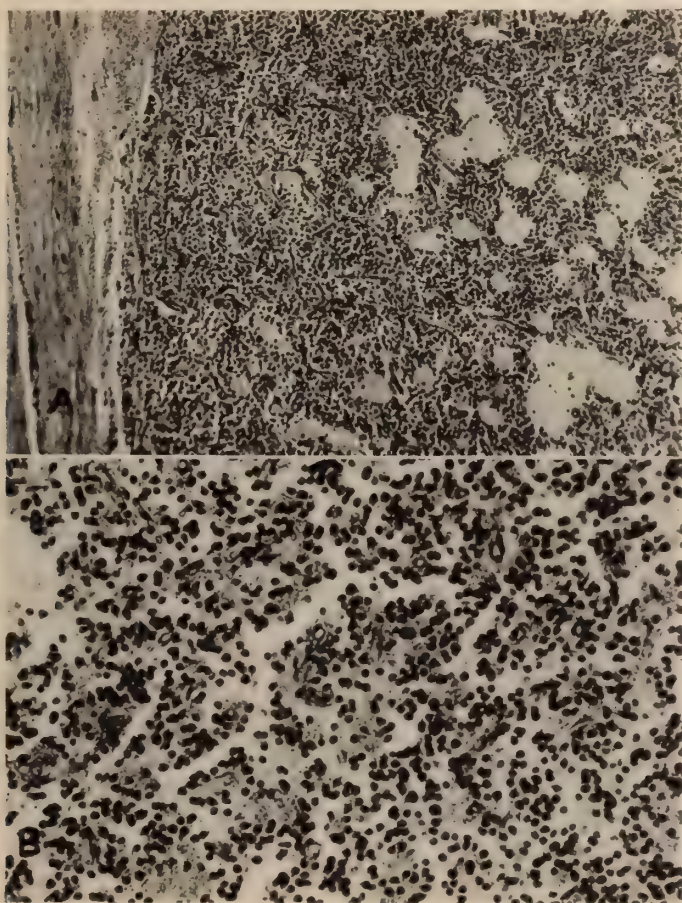


FIG. 2 (Case 1). A. Low power magnification demonstrating the sharp demarcation of the tumor from the surrounding tissue. B. High power magnification showing cell masses with a tendency to acinar configuration.

aches recurred, now accompanied by nausea and vomiting. The patient re-entered the hospital on July 8. He was somewhat apathetic and the neurological findings were as previously noted. An exploratory craniotomy was performed but no neoplasm was found. The patient lapsed into coma and died three days subsequently, on July 11, after an illness of eight and one-half months.

Necropsy Findings. Gross Anatomy. The brain showed evidence of increased intracranial pressure. A large well circumscribed tumor was found in the enlarged left lateral ventricle protruding through and occluding the foramen of Monro. It extended from the anterior horn to the middle of the body of the ventricle, projecting into the third ventricle as far back as the Sylvian aqueduct.

Microscopic Anatomy. The tumor was very cellular, being made up of small round cells. In some areas the cells, set in a vascular stroma, were grouped in dense masses with no particular pattern, but in other regions an acinar, glandular-appearing arrangement was present. No mitotic figures were seen. Mucin stains were negative.

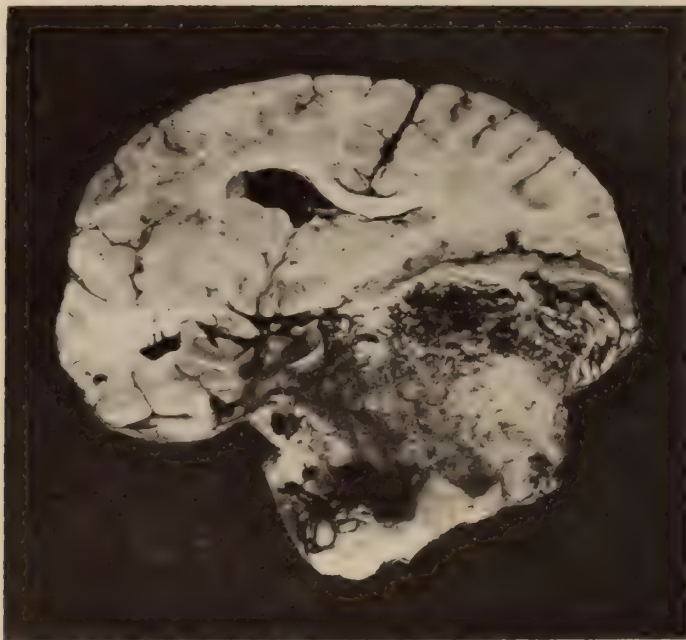


FIG. 3 (Case 2). Appearance of the tumor in coronal section showing distortion and shift of the ventricles.

Comment. The presence of rigidity and Parkinsonian tremors suggested the diagnosis of encephalitis. However, the encephalogram pointed to the existence of a neoplasm. The failure of any air to enter the left lateral ventricle was due to the fact that it was almost completely filled by tumor which occluded the foramen of Monro. Histologically, the tumor may be described as a cellular ependymoma, although certain areas showed an acinar structure.

Case 2. History (Adm. 406660). A 2 year old female infant was well until two months before admission when she began to vomit about three

times weekly. Following an upper respiratory infection one month later, she became increasingly listless and drowsy. Trembling of the left hand was noted when she attempted to grasp objects.

Examination. The patient was a well nourished but apathetic and disinterested child, who cried when handled. However, at times, she responded adequately and showed no mental impairment. The occipital

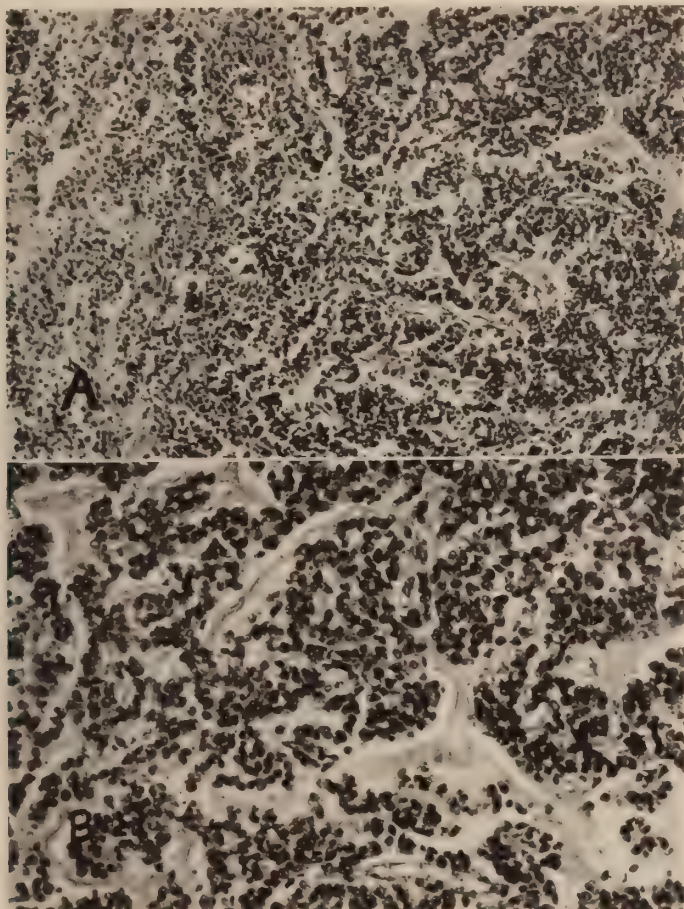


FIG. 4 (Case 2). A. Histologic appearance of the tumor under low magnification. B. High power magnification showing acinar cell aggregations.

region of the skull appeared prominent and was tympanic on percussion. There was ataxia and an intention tremor of the left hand and she seemed unable to bear her weight on the right lower extremity. Both right extremities were hypotonic and paretic. The abdominals were absent and a right Babinski sign was obtained. Bilateral papilledema was marked with an intermittent left external strabismus.

Course. Ventriculography showed a marked dilatation of the third and left lateral ventricles with displacement to the left. The pineal gland was shifted inferiorly and posteriorly. Tissue obtained from the eye of the ventriculography needle was described histologically as coming from the neighborhood of a primary neuro-ectodermal tumor. The child reacted poorly following this procedure and died three days later with hyperpyrexia.

Necropsy Findings. Gross Anatomy. A hard, brownish-yellow tumor was found extending throughout the right occipital and parietal lobes and into the right temporal region. The left lateral ventricle was dilated and the entire ventricular system was displaced to the left. The di-

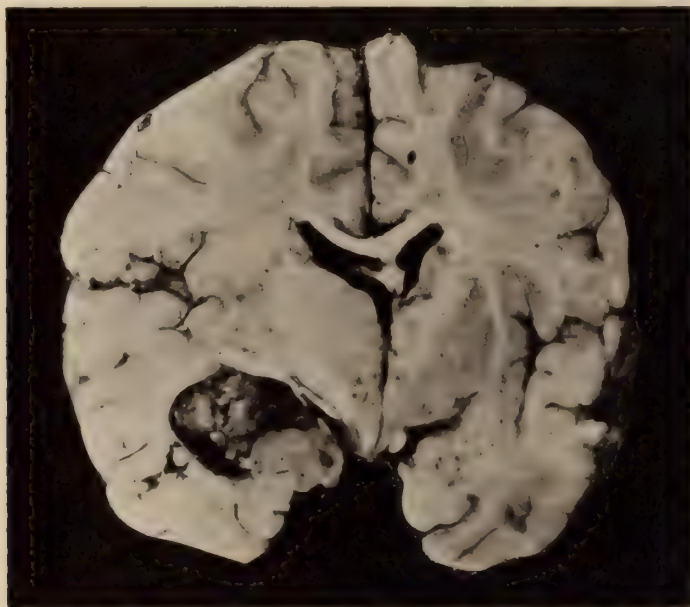


FIG. 5 (Case 3). Tumor occupying the right occipital horn

encephalon and midbrain were compressed. The pineal gland was present and intact.

Microscopic Anatomy. The tumor was composed of densely cellular tissue, containing large, predominantly oval-shaped nuclei. These were separated into aggregations by strands of highly vascular connective tissue. In certain areas the cells assumed an acinar or papillary structure. Numerous compound granular corpuscles were seen. There was no line of demarcation between the tumor tissue and the adjacent brain substance. Muci-carmin stains did not reveal the presence of mucin, nor did glial preparations throw any additional light on the nature of the tumor.

Comment. The presence of an intracranial tumor was confirmed by

ventriculography. Surgical intervention would have been unavailing because, unlike most ependymomas, the tumor had invaded the adjacent brain substance over a wide area.

Case 3. History (Adm. 332952). A three year old child was admitted to the hospital on December 4, 1931 in a moribund condition with a three-

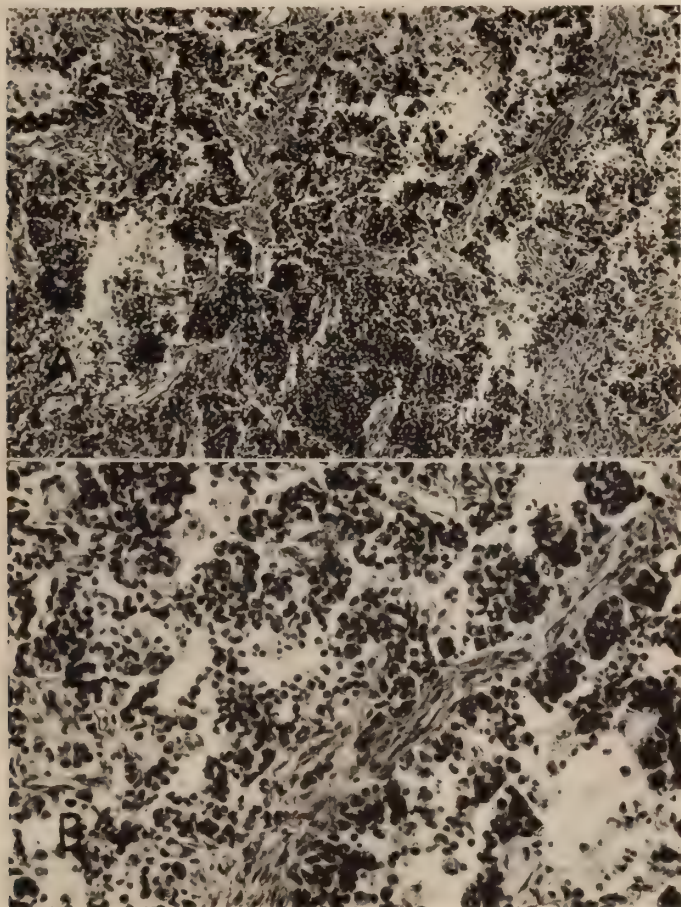


FIG. 6 (Case 3). *A.* Appearance of the cell masses under low magnification. *B.* High power magnification. The cellular aggregations are separated by connective tissue septa.

week history of vomiting, abdominal pain and headache. Inward rotation of the left eye had also been observed. In the twenty-four hours preceding admission the child had four tonic convulsions with the appearance of stiff neck and dysarthria.

Examination. The patient was in a deep stupor. The extremities

were flaccid with complete areflexia. The pupils were dilated and fixed to light. There was bilateral papilledema. Lumbar puncture disclosed a xanthochromic fluid containing 20 lymphocytes.

Course. The child could not be aroused and died in a few hours.

Necropsy Findings. Gross Anatomy. The entire ventricular system was displaced to the left. There was a moderate internal hydrocephalus, greater on the right. A soft necrotic tumor mass filled the posterior two-thirds of the posterior horn of the right lateral ventricle and extended into the body. It was attached to the ependymal lining at several points. At the occipital pole it appeared to have eroded through to the surface in the region of the calcarine fissure.

Microscopic Anatomy. The tumor consisted of large masses of cells in a fibrous stroma. The individual cells were round and had reticular nuclei. The masses were, for the most part, clustered together without

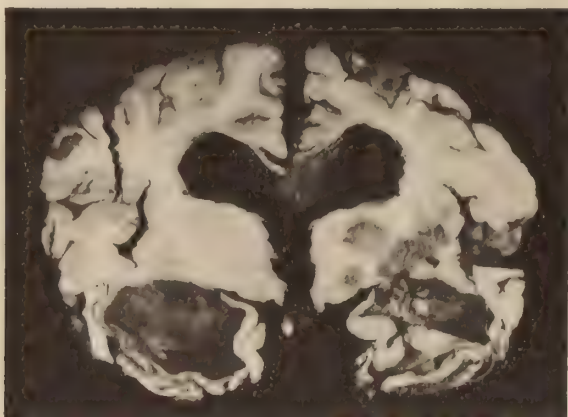


FIG. 7 (Case 4). Coronal section of the brain showing internal hydrocephalus and tumor occupying the right posterior horn.

a particular pattern, but some tended to assume an acinar arrangement. Many mitotic figures and occasional giant cells were observed.

Comment. The presence of a tumor within the ventricular system, undergoing necrobiosis and liberating disintegrating blood, accounts for the xanthochromic cerebrospinal fluid. The vomiting and the neck rigidity suggested the probable existence of a meningeal process, readily explained by the presence of xanthochromia in the cerebrospinal fluid. The abdominal pain may possibly have been a cerebral manifestation. The tumor showed a varied histological structure with a great predominance of immature cells and many mitotic figures. The connective tissue stroma was similar to that shown in the more advanced types of papillary ependymomas.

Case 4. History (Adm. 233278). A 10 weeks old male infant was well until seven days before his admission to the hospital on August 16, 1923. At that time he began to vomit after each feeding and held his head in a retracted position.

Examination. The head was enlarged and held in hyper-extension. The fontanelles were tense and there was a positive Macewen's sign. The infant was irritable when handled. A convergent strabismus was present and transient stiffening of the right extremities was observed. Lumbar puncture disclosed clear fluid under increased pressure containing 60 lymphocytes.

Course. Repeated lumbar punctures were performed since it was believed that the child was suffering from meningitis. It lost weight and vigor and died on August 28, 1923.

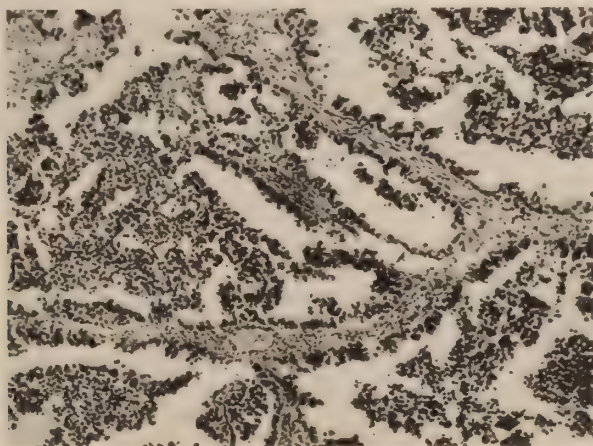


FIG. 8 (Case 4). Low power magnification. The papilliform structure resembles that of the choroid plexus.

Necropsy Findings. Gross Anatomy. There was a large internal hydrocephalus which involved the lateral and third ventricles and aqueduct of Sylvius. The posterior horn of the left lateral ventricle was completely filled by a large reddish-brown mass, the whole of which could be readily enucleated.

Microscopic Anatomy. The tumor contained many papillomatous structures lined by ependymal cells with a vascularized connective tissue core resembling the normal picture of the choroid plexus. There were also simpler acinar forms and cells grouped in large masses. Mucin was observed both intra- and extra-cellularly.

Comment. The rapid course and pleocytosis in the spinal fluid gave presumptive evidence of meningitis, which is understandable when the intimate association of the tumor with the ventricular system is considered. The tumor showed the mature structure of the choroid plexus.

Case 5. History (Adm. 291491). A 14 month old male infant was admitted to the hospital on June 4, 1928. Following a right mastoidec-

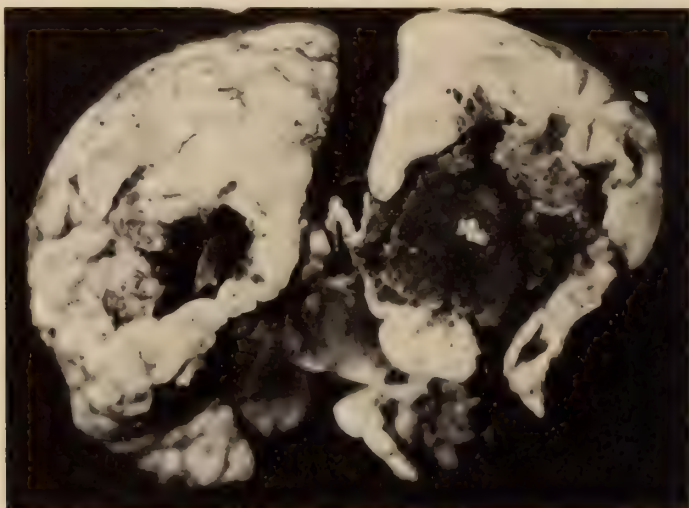


FIG. 9 (Case 5). Gross appearance of the large necrotic tumor in the posterior portion of the right lateral ventricle.

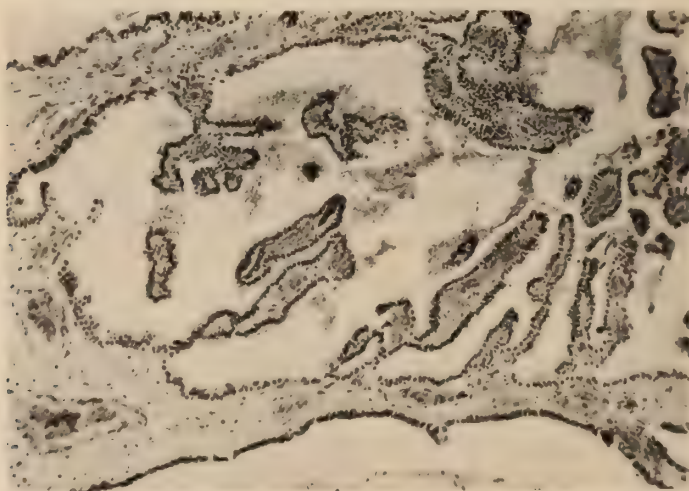


FIG. 10 (Case 5). Low power magnification of the tumor reduplicating the pattern of the choroid plexus.

tomy several weeks previously, the patient had become listless and irritable and had vomited several times daily.

Examination. The infant was apathetic and listless. There was marked hydrocephalus. Deep reflexes were exaggerated on the left side

and there was a left facial weakness. The eyeballs were turned upward and to the right. The pupils reacted poorly. Lumbar puncture yielded a clear, colorless spinal fluid under increased pressure.

Course. The infant developed a pneumonia and died several days after admission.

Necropsy Findings. Gross Anatomy. The lateral and third ventricles were distended. On the roof of the aqueduct of Sylvius was a large arachnoid cyst which reduced the tectum to a thin membrane and displaced the aqueduct to the right. A brownish, friable, well-circumscribed tumor mass filled the posterior horn of the right lateral ventricle.

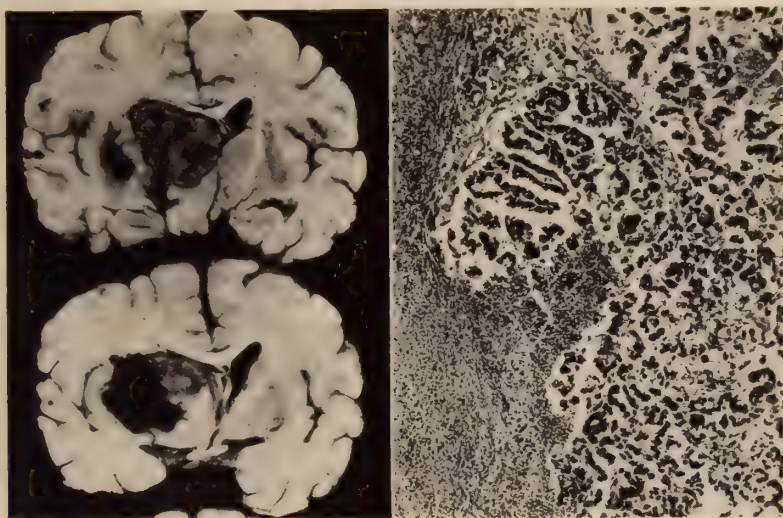


FIG. 11 (Case 6). A. Coronal sections of the brain showing the well encapsulated neoplasm filling the entire body of the left lateral ventricle. B. Histologic appearance of the tumor with acinar and papillary cell configuration.

Microscopic Anatomy. The tumor duplicated the structure of the choroid plexus presenting typical papillae lined with columnar epithelium. Mucin was not found.

Comment. The presence of hydrocephalus and high cerebrospinal fluid pressure accompanied by left-sided signs indicated a neoplasm in the right cerebral hemisphere. Histologically, the tumor was of a mature villous variety.

Case 6. History (Adm. 411470). A 45 year old watchman was admitted to the hospital on July 14, 1937 with a seven months' history of severe and throbbing headaches. There had been a progressive personality change, the patient having become slovenly and indifferent; and in the three weeks preceding admission he had become mentally confused.

Examination. The patient was aphasic; he had especial difficulty in finding words. He perseverated, had trouble in distinguishing left and right and appeared generally confused. His memory for all events was poor. Neurologically, there was a right supranuclear facial weakness. The right upper extremity was paretic and exhibited a "grasp phenomenon." Abdominal reflexes were absent. Deep reflexes on the right side were exaggerated with a positive Babinski sign. Lumbar puncture revealed xanthochromic fluid under a pressure of 310 mm. of water.

Course. Ventriculography showed an internal hydrocephalus, more marked in the anterior portions of the ventricles. There was a shift to the right. Exploratory craniotomy through a left frontoparietal flap revealed a neoplasm. The patient died four days later with a bronchopneumonia.

Necropsy Findings. Gross Anatomy. There was an internal hydrocephalus. A large granular, mottled, well encapsulated neoplasm filled the entire body of the left lateral ventricle. The third and right lateral ventricles were displaced to the right. The tumor bore remnants of the choroid plexus on its surface. Posteriorly it projected into the transverse fissure.

Microscopic Anatomy. The tumor reduplicated the pattern of the choroid plexus containing villous tufts covered by ependymal cells. Mucin was found intracellularly and extracellularly.

Comment. The clinical course was not indicative of the presence of a ventricular tumor, although the xanthochromic spinal fluid could have suggested its existence. Histologically the core of the papillae contained numerous blood vessels. This vascularity favored extravasation of blood into the ventricles, resulting in xanthochromia.

DISCUSSION

Tumors, such as those arising from the choroid plexus and those forming from ependymal lining, have been reported by Cushing and Davis (2) and Bailey (3). Though recognizing their common origin these authors stressed the differentiation of the choroid from the ependymal cells. They also described the glial framework of ependymomas as contrasted with the connective tissue core of papillomas of the choroid plexus. They further emphasized the presence of "blepharoplasten," tiny granules in the cells of ependymoma, a feature which Mallory (4) originally pointed out as a means of distinguishing ependymomas from other glial tumors. Bailey, however, showed that these blepharoplasten might also be found in some pineal and subependymal cells and hence could not be regarded as specific for ependymomas. The Kernohans found that many of the ependymomas in their series lacked these blepharoplasten. In none of the cases herein presented could these granules be demonstrated. The Kernohans also pointed out that not only the papillomas of the choroid

plexus but many of the ependymomas, especially the papillary types, had a mesodermal rather than a glial core.

Ependymomas are most commonly found in children. (Four of the six cases here reported occurred in infants.) They frequently show calcification. In 45 per cent of the cases reported by List (6) calcification was demonstrated roentgenologically. Grossly, these tumors are usually well demarcated, if not encapsulated. In only one of our six cases was the cerebral substance invaded. At times, by virtue of their discreteness and only partial attachment to brain substance they offer a good chance for surgical intervention, but their location in the recesses of the ventricular cavities makes operation extremely hazardous.

From a diagnostic standpoint a study of the clinical features of the cases presented suggests that, when cerebral neoplasm is suspected in a child who reveals meningeal signs and xanthochromic fluid, an ependymoma should be seriously considered.

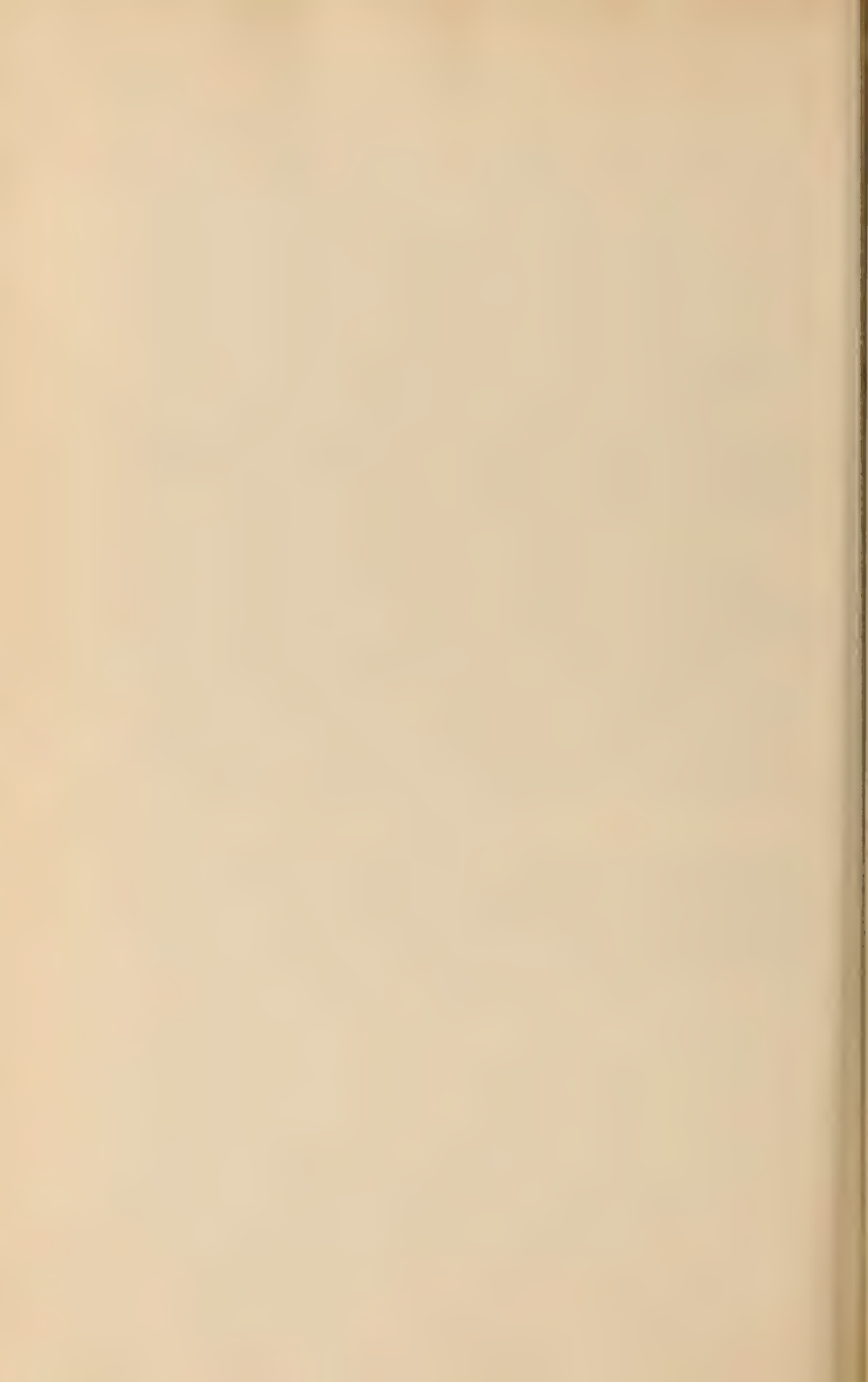
CONCLUSIONS

1. Six cases of ependymal tumors are reported.
2. The ependymal cells of the choroid plexus and ventricular lining have a common embryological derivation.
3. Ependymal tumors tend to assume a papillary structure ranging from an acinar grouping of cell masses to a reduplication of the pattern of the choroid plexus.

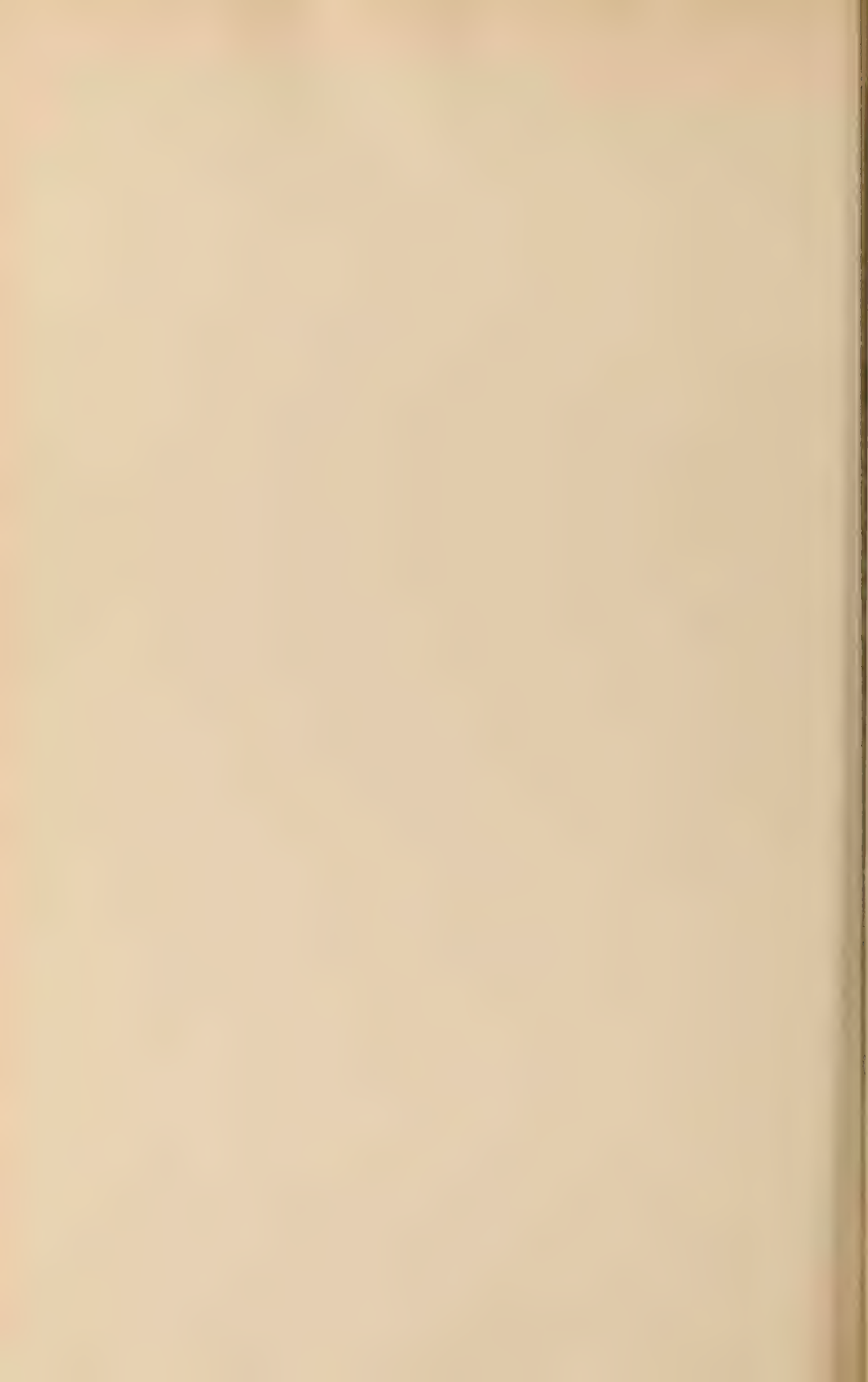
I wish to express my sincere appreciation to Doctor Joseph H. Globus, under whose supervision this work was carried out.

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ERRATUM

JOURNAL OF THE MOUNT SINAI HOSPITAL

In the article, "Graphic Rigidity Index" by Dr. Lewis J. Doshay, published in the November-December issue of the journal (Volume V, Number 4), Graph 3 on page 456 is inverted.



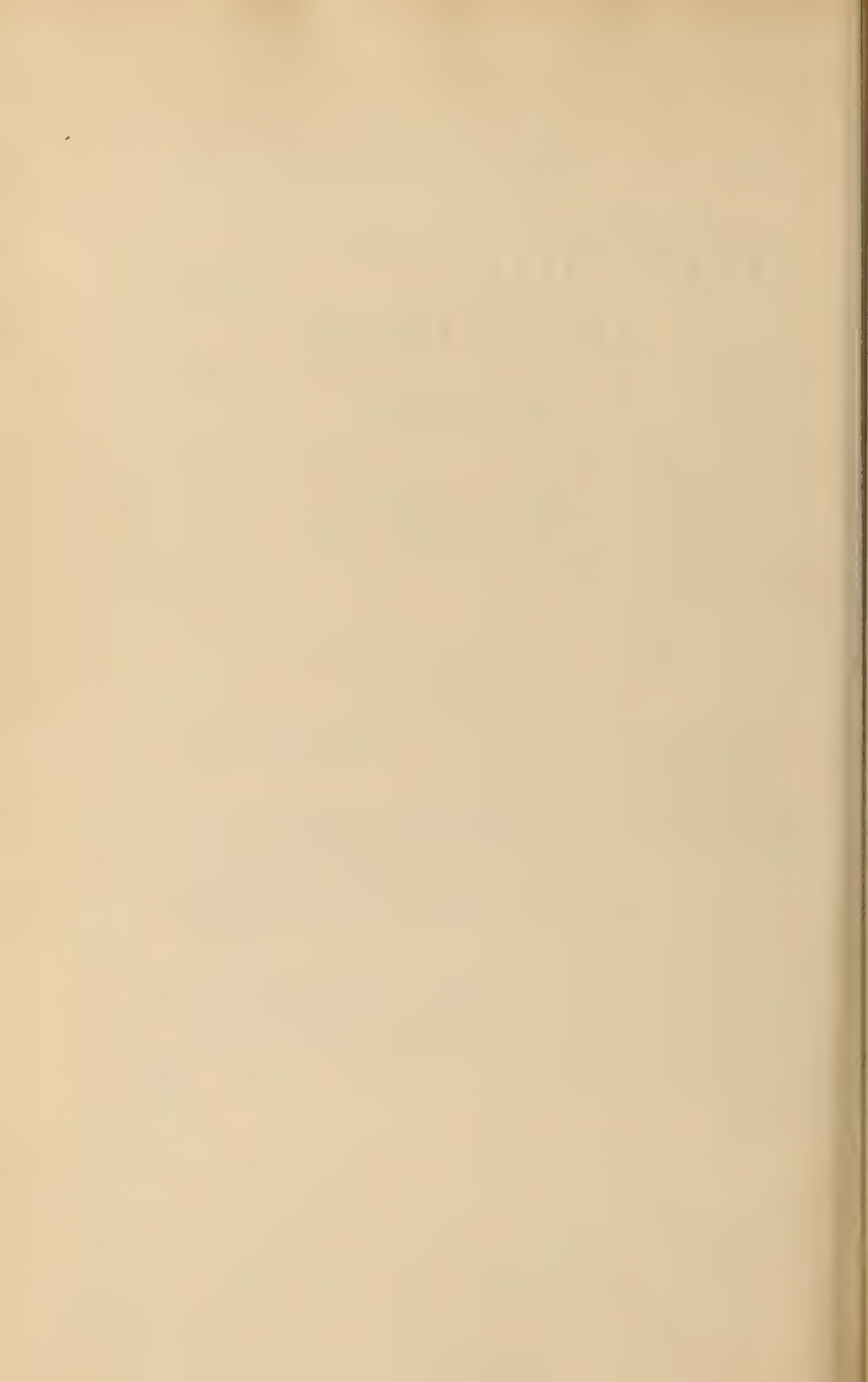
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THE WILLIAM HENRY WELCH LECTURES

I. SOME NEW ASPECTS OF HOMEOSTASIS¹

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Our bodies are composed of extraordinarily unstable material. Muscles are made to contract by almost incredibly minute nerve impulses; it has been estimated that the energy of a single impulse is related to the energy of the consequent muscular twitch as 1/200,000. The olfactory surface has long been known to be marvelously sensitive; by means of it we can perceive the presence of mercaptan in a dilution of 1/23,000,000 of a milligram diffused in a liter of air. And the retina is reported to be three thousand times more delicately responsive than the most sensitive photographic plate. Further evidence of the instability of living structure is found in the common experience of fainting. Even a slight check of the blood supply to some nerve cells of the brain abolishes consciousness, and total anemia for eight or nine minutes may result in irreparable injury of such cells.

When we consider the extreme instability of parts of our body structure, their readiness for disturbance when only slight external forces are applied, and their rapid deterioration in the absence of favoring conditions, the persistence of the normal state and normal activity through many decades seems nothing short of miraculous.

When we consider further that our organisms form an open system, engaging in a free exchange of material with the outer world, and that the bodily structure itself is not permanent but is being continuously broken down with every action and continuously built up by the process of repair, the wonder of persistent normality and function increases.

The ability of higher organisms to maintain a fairly constant state has long impressed biologists. The idea that corrective agencies are present in living beings is at least 2,300 years old. Centuries ago that idea was expressed in the phrase, "*vis medicatrix naturae*"—the recognition of a factor or factors restoring the normal state when that has been disturbed. In recent times eminent physiologists—Richet, Pflüger and Fredericq—have emphasized this remarkable phenomenon. Indeed, Fredericq (1) declared that the higher the position of an organism in

¹ Delivered at The Blumenthal Auditorium, The Mount Sinai Hospital, New York City, May 18, 1938.

the scale of living beings the more numerous, the more perfect, and the more complicated are the corrective agencies.

An important contribution toward understanding the phenomenon of organic stability was offered by Claude Bernard (2) about ninety years ago. He pointed out that, as living beings, we have not only the same external environment as other objects but also an "internal environment." In a sense we are not air-inhabiting animals, for we are separated from the surrounding air by a layer of dead stuff, the horny scurf of the skin and the moisture of the mucous membranes. All that is alive within these lifeless coverings is in contact with fluid. Indeed, our living parts may be conceived as bathed by a watery solution of salts and colloids—the blood, the lymph, and tissue fluids. It is these fluids which form a *milieu interne*, as Claude Bernard expressed it, or a fluid matrix, as I prefer to call it.

Just in so far as the internal environment, or fluid matrix, is kept constant are we independent of limiting changes in the external environment; we carry with us always our own personal atmosphere. Also we are independent of the disturbances of the internal environment that are produced by our own actions. The freedom which is thus assured is a privilege of the higher vertebrates, birds and mammals. We have evidence that in the process of evolution the devices assuring a constant state were only gradually achieved. For example, the frog, in which control of body water and temperature is lacking, is limited in the summer to the vicinity of a moist region and in the winter must sink to the bottom of a frigid pool; only when the warmth of spring returns is he freed from the paralyzing effects of the icy water. Birds, on the contrary, with their feathery covering, may spend the winter in vigorous activity because of special devices for keeping warm.

The constancy of the fluid matrix is controlled by the organism itself. In that control many complex physiological processes may be involved. The term "equilibrium," which is technically applied to simple physical and chemical systems, is not adequate to express the complicated arrangements in the body for preserving uniformity. I have suggested, therefore, that the relatively stable state maintained in the fluid matrix should be given the special name, "homeostasis" (3).

During the past nine years investigators in the Harvard Physiological Laboratory have presented evidence that the sympathetic division of the autonomic nervous system plays an important rôle in controlling the homeostatic devices of the body. Almost all the studies, however, were made on cats. Recently our evidence has been questioned, mainly by C. Heymans (4) and his collaborators, because of effects which they have observed on sympathectomized dogs. Whereas the sympathectomized cat, when exposed to exacting conditions, showed notable deficiencies, the sympathectomized dog exposed to similar conditions was hardly

distinguishable from the normal dog. The cat and the dog differ, however, in their natural habits, one being relatively sedentary, the other remarkably active. In the present lecture I propose to compare these two as animal types, when normal and when deprived of the sympathetic nerve supply, and incidentally to review the evidence for homeostatic control of the fluid matrix. Also I propose to consider an extension of the concept of homeostasis.

As an introduction to the facts which will be presented, may I remind you that the sympathetic division of the autonomic nervous system is connected with the central nervous axis between the brachial and the sacral enlargements of the spinal cord, and that it consists mainly of two ganglionic chains reaching from high in the neck to the pelvis, one on each side of the midline, close to the spinal column. From these ganglia postganglionic fibers pass out to the smooth muscles of blood vessels and hairs, to sweat glands and to other glands (including the adrenal medulla), and also to the heart. It is quite possible to remove the ganglionic chains in whole or in part. When a cat, for example, is thus operated upon it continues its existence indefinitely in the confines of the laboratory where food is provided, temperature is regulated, and the struggle for existence is minimal. Deficiencies appear only when the constancy of the fluid matrix is in danger. These deficiencies are various. At present I propose to consider those that become manifest upon exposure to heat and cold, to the possibilities of insufficient oxygen, and to a low concentration of blood sugar.

Exposure to Cold. When the sympathectomized cat is placed in a cold environment the hairs do not rise and enmesh a layer of protective air around the body. Furthermore, there is no narrowing of the surface blood vessels to check the distribution of warm blood to the cold skin. Still another defect is the failure of secretion of adrenine from the adrenal medulla. A small amount of this remarkable substance, one milligram, injected subcutaneously, will accelerate the metabolic processes of the body, as shown by Boothby and Sandiford (5), to the extent of producing fifty extra calories. Without the sympathetic the advantage of this extra heat production is lost. In such circumstances, sympathectomized cats left in an environment of approximately $5^{\circ}\text{C}.$, are demonstrably less able than normal cats to maintain the ordinary level of body temperature. Their temperature may drop as much as $2.5^{\circ}\text{C}.$ within two hours, in spite of vigorous shivering. The shivering, of course, produces extra heat in the body but by itself it is usually ineffective in preserving temperature homeostasis.

When Heymans and his collaborators reported that there was no noteworthy deficiency of sympathectomized dogs if exposed to cold, they based the statement on incidental observations. They did not record careful attention to the temperature of the air nor to the temperature of the dogs

In recent studies in the Harvard Laboratory, carried on by Dr. McDonough (6), dogs of similar hair coat and size were compared, as normal and as sympathectomized animals. They were exposed to temperatures of approximately 5°C . Under these conditions, not only the sympathectomized but also the normal dogs shivered vigorously (normal cats rarely shiver at 5°). Records of shivering revealed that in the normal animals the rate was in the neighborhood of 400 muscular contractions per minute. In the sympathectomized dogs it was approximately 50 per cent higher. Despite the higher rate, however, there was a fall of body temperature in the sympathectomized animals. It was not so great a fall as was observed in cats deprived of the sympathetic system, being only about 0.5°C ., but it was typically present. From these observations we may conclude that because of its service in lifting the hair, in contracting surface vessels and discharging adrenaline, the sympathetic system is useful to dogs as it is to cats in maintaining a stable state. When the system is absent the animals resort to shivering sooner and more vigorously than do normal animals. The dog, however, differing from the cat in being much more muscular, produces more heat in shivering. Furthermore, even in his normal state he is accustomed to shivering as a means of maintaining a homeostasis of temperature. For these two reasons we can explain the greater effectiveness of the dog as compared with the cat in a cold environment after the sympathetic system has been removed.

Exposure to Heat. When warm-blooded animals, having sudorific glands, are exposed to a high temperature, homeostasis is preserved by the secretion of sweat which, on evaporating, cools the skin, and also by superficial vasodilation which allows the warm blood to lose heat to the cool skin. Both sweating and dilation of the blood vessels are under control of the sympathetic system. Also panting may be used, which provides an evaporation from the upper respiratory passages and thereby a cooling of the fluid matrix, as represented in the flowing blood. Panting is made especially effective, of course, by evaporation of saliva.

When sympathectomized cats are exposed to a warm atmosphere sweating is impossible. There is a possibility of vasodilation in these animals, but whether it occurs is undetermined. In cats, panting is a rare mode of regulating body temperature. When, therefore, sympathectomized cats are placed in warm surroundings (about 40°C .) they are readily shown to have a defective temperature control. The temperature may rise a full degree (C .) higher in these animals than in normal cats in the same circumstances (7).

When sympathectomized dogs are compared with normal dogs having similar hair coats and undergoing exposure to the same moderate heat for the same length of time, the body temperature may indeed rise somewhat higher in the animals operated upon than in the normal. The increase, however, is negligible. Again the dog is revealed as an extraordinarily

efficient organism despite the absence of the sympathetic system. This superiority of the sympathectomized dog as compared to the sympathectomized cat when in a warm environment is explained by the remarkable accessory devices possessed by the dog in his great tongue and lavish discharge of saliva. The dog promptly resorts to panting when his temperature tends to rise. By the evaporation of saliva (a parasympathetically controlled secretion not interfered with by sympathectomy) heat is removed from the tongue and mouth where the blood abundantly circulates. Thus the body temperature is kept from rising. This striking accessory mode of avoiding a rise of body temperature is associated with the greater activity of the dog as compared with the cat. The dog is characteristically an active animal, running uninterruptedly for long distances and producing through muscular exertion a large amount of heat. The cat is typically a quiet animal, capable only of quick, short spurts of running. Since the dog has sweat glands only on the nose and toe pads, panting and a great outflow of saliva for evaporation become the chief means of heat loss—a means which is rarely employed by the cat.

The Acid-base Balance. The fact is familiar that the reaction of the blood is slightly alkaline—whereas a pH of 7 is neutral, the blood on the alkaline side of neutrality is expressed by a pH of 7.4. Close to that figure it is ordinarily held by the homeostatic factors; it may become further alkaline, to 7.8, whereupon convulsions may occur, or it may be reduced very slightly below 7.0, whereupon coma supervenes. In vigorous muscular work a large amount of non-volatile lactic acid is produced, an amount which would soon overwhelm the alkaline buffer in the blood. The danger of coma which might result is avoided by a supply of extra oxygen to the active tissues, where the lactic acid may be burned to volatile carbonic acid and then breathed away through the lungs. In the process of supplying the extra oxygen the organs controlled by the sympathetic system come into service. The heart is made to beat more rapidly, the blood pressure rises, and by contraction of the spleen extra erythrocytes are pressed into use in the circulation. With a higher head of arterial pressure the rate of blood flow between the lungs and active organs is increased. By this faster flow and the greater number of red corpuscles in the circulating stream the delivery of oxygen is greatly augmented. Associated with these changes, brought about through sympathetic control, there is an increase of respiration. This assures a larger supply of oxygen in the lungs and a more rapid removal of carbon dioxide from them.

When the sympathectomized cat engages in even moderate muscular activity it is instantly revealed as a very defective animal. The arterial pressure, instead of rising, actually falls, and if the cat attempts to run it is likely to faint (8). It is therefore incapable of prolonged or vigorous action. The fall of pressure is due to vasodilator impulses carried to the arterioles over non-sympathetic pathways. When the depressor points

in the medulla of a sympathectomized cat are stimulated the blood pressure drops (9); and if the nerves of the carotid sinus are stimulated they likewise will produce, in the cat without a sympathetic system, a lowering of arterial tension.

The conditions in the dog are different to a very noteworthy degree. Whereas the cat has relatively few sympathetic dilator nerves and quite effective non-sympathetic dilators, the dog, with strong dilator influences in the sympathetic, is weak in the non-sympathetic supply. Stimulation of the carotid sinus nerves does not lessen arterial tension in the sympathectomized dog (4). The consequence is that the dog, deprived of the sympathetic system, may not suffer any drop of blood pressure on engaging in activity, but instead, a rise. Thus fortified against the dangers of vascular hypotension, the dog, though lacking sympathetic nerves, is capable of running, playing, jumping, and fighting almost as efficiently as the normal animal (10). The remarkable muscular activity of the sympathectomized dog, as contrasted with the sympathectomized cat, is further accounted for by the presence, in the vagus nerves in the dog, of cardio-accelerator fibers, capable of raising the heart rate to a greater degree than is reached by mere abolition of vagal tone (11).

It is difficult to compare quantitatively the ability of the dog and the cat to work, because the cat is not an animal easily trained to exercise. Many of the physiological devices that are used in running, however, are brought into action when animals are exposed to a low concentration of oxygen or to a high altitude. It is possible to compare normal and sympathectomized cats and also normal and sympathectomized dogs in their endurance of low oxygen tensions. When such a test is applied a striking difference is found between the two species of animals, whether normal or sympathectomized. The normal cat, exposed to an atmosphere containing 8 per cent oxygen, as contrasted to the usual percentage of approximately 21, will endure the test for about an hour. Sympathectomized cats, on the other hand, faint or collapse in a relatively short time, occasionally within fifteen or twenty minutes (12). Normal dogs, however, will live in an atmosphere of approximately 4 per cent oxygen for more than two hours before manifesting, by a change to slow breathing, that they are in danger. If sympathectomized dogs are exposed to similar concentrations of oxygen they are shown not to be so hardy. In six cases this low oxygen tension was endured for an hour and a half by four of these animals, and approximately two hours by the other two (6).

In reviewing the observations which have thus far been detailed we note that the dog lacking the sympathetic system is much more efficient in critical situations than is the sympathectomized cat. The dog withstands heat, cold, muscular work and lack of oxygen much better than the cat. These facts do not prove, however, that the sympathetic system is unimportant for homeostasis. The sympathectomized dog is, indeed, less

capable than the normal dog when subjected to stress, but he is not rendered by the operation of sympathectomy as defective as the cat. These observations emphasize the fact that the dog has very remarkable accessory homeostatic mechanisms. They are associated, as I interpret them, with the dog's extraordinary activity. If a young dog accompanies us on a walk in the woods or fields he traverses perhaps three or four times the distance that is walked, and furthermore, does it on the run. One rarely if ever goes walking with a cat! The dog as a running animal necessarily produces much heat. Associated with that consequence of his vigorous movements he has, lacking abundant sweat glands, a special ability to discharge heat by panting. A long, large tongue, well supplied with blood and abundantly provided with saliva, makes panting an effective agent for heat loss. Only as a last resort does the cat make use of the panting mechanism. In resisting cold, the dog is likewise exceptional. He shivers readily, and when he is in a cool environment he resorts to this source of heat. Because of his great muscular development he has special power for producing heat by the shivering process. Finally, as a running animal the dog requires an abundance of oxygen to burn the lactic acid produced by his lusty muscular activities. All the devices for supplying oxygen to the tissues are much more developed in the dog than in the cat. The dog's chest, for example, is deep and capacious compared with that of the cat. In relation to body weight his lungs are about twice the weight of the cat's lungs. The blood weight of the dog is approximately 8 per cent of the body weight, whereas in the cat it is approximately 5.5 per cent (13). On the human scale the dog's hemoglobin is 94 per cent, whereas the cat's is 56 (14). The canine heart is large; in relation to body weight it may be two or three times the weight of the feline heart (15). Note that the remarkable lung capacity of the dog and his high hemoglobin percentage are not lessened by sympathectomy. There is evidence that his blood volume is actually increased by removal of the sympathetic system (16). In this group of functions concerned with delivery of oxygen to active organs the heart rate alone might be affected by removal of sympathetic accelerators; but the dog has vagal cardio-accelerators. Furthermore, the non-sympathetic vasodilator nerves are unimportant in the dog, and consequently he does not suffer from a fall of arterial pressure when the sympathetic is removed. After sympathectomy, therefore, these accessory homeostatic devices come prominently into play. Shivering, for example, as we have seen, is much more rapid than in the normal animal. It is because the dog is provided with these extraordinary adjuvant homeostatic mechanisms that he is less affected than the cat when deprived of the regulatory functions of the sympathetic system.

The interesting question arises as to whether man is nearer the cat or nearer the dog in his physiological abilities. It seems probable that the young man in athletic condition is much nearer to the dog than the cat

in possessing excellent homeostatic functions. Doubtless a man would suffer more from removal of the sympathetic system than does the dog, because he depends on sweating for temperature control when excessive heat is produced by muscular exertion or when he is exposed to high external heat. He does not ordinarily make use of panting. Since sweating is under sympathetic control, man would obviously be at a definite disadvantage compared with the dog in the critical state of a rising body temperature.

There are, to be sure, bodily conditions in which the special provisions which the dog enjoys as a running animal cannot compensate in maintaining homeostasis. One of these is seen in the general response of organisms to the hypoglycemia produced by insulin. Normally, secretion from the adrenal medulla is pre-eminently the agent for liberating glucose from the liver (17). If the adrenal glands are intact and receiving sympathetic impulses, and insulin is given in such a dose as to cause the blood sugar to fall, at a critical point in the fall the sympathetic system will be brought into action (18). Adrenine will be secreted into the blood stream—as disclosed by the faster beat of the denervated heart—and the drop in blood sugar will be checked. The injection of glucose into the blood stream will promptly stop the extra discharge of adrenine from the adrenal medulla. If the adrenal glands, however, are no longer under nervous control, as in the sympathectomized animal, the same test will result in a progressive hypoglycemia—there will be no adrenal secretion, as shown by failure of acceleration of the denervated heart, and the drop in the glucose concentration of the blood will not be checked.

When normal cats are subjected to a standard dose of insulin (0.5 unit per kilogram) there is commonly no reduction of blood sugar to the convulsive level, and if it is reduced to that level, the effect is belated. In sympathectomized cats, on the contrary, the same dose produces convulsions in some instances, or, if not convulsions, very serious conditions from which the animals must be rescued by glucose injections (19). The same phenomena are observed in contrasting normal and sympathectomized dogs. A dose of insulin (0.5 unit per kilogram) which does not produce convulsions in the normal animals results in convulsions or collapse in the sympathectomized, from which they must be rescued by receiving glucose (6). In these circumstances it is obvious that the sympathetic system as a homeostatic regulator is quite as important in the dog as it is in the cat.

Now I wish to consider with you an extension of the concept of homeostasis. Originally the idea was associated with constancy of the fluid matrix as a whole, that is, to the relatively uniform state of the blood and lymph throughout the body. The value of this uniformity of the *milieu interne* was conceived by Bernard, Fredericq and Richet, as resulting from stable states throughout the organism. We must recognize, however,

that there are provisions for preserving constancy of local conditions in the body. A few examples will make the meaning clear.

When muscles become active, as Krogh (20) has shown, many capillaries which are collapsed during muscular rest are opened and serve as effective carriers of oxygen; they may be from forty to one hundred times as numerous in the contracting as in the resting muscle. Observations have shown that the blood flow may be five times as great through the active muscle as it is through the inactive. This especially faster flow in a region of high metabolism supplies the extra oxygen and the energy-yielding material required for the more vigorous chemical processes which are taking place. Furthermore, the faster flow more effectively carries away the extra waste materials which result from the chemical processes. In times of need, therefore, there are arrangements for local homeostasis, i.e., for local preservation of uniform conditions (16).

Another illustration is found in the blood supply of certain endocrine glands. These glands secrete substances which might be highly concentrated at the source unless there were special devices for dilution. Unfortunately we do not know about the blood flow in many of the endocrine organs. We have information, however, concerning the thyroid and the adrenals. The circulation in these glands, when calculated for standard conditions and for unit weight of the organs, is revealed as many times that of other organs (21). Again we note an arrangement for local homeostasis.

There are also special provisions for essential and peculiarly sensitive structures. Notable among them are the very delicate neurones of the cerebral cortex and the muscle of the continuously active heart. Unless a sufficiently high arterial pressure is present the delivery of oxygen to the organs of the body will be inadequate. In a falling blood pressure a critical level is reached at approximately 70 mm. of mercury. Below this level the alkaline buffers of the blood begin to be neutralized by non-volatile acid, as revealed by reduction of the carbon-dioxide capacity, and also by decrease of the metabolic rate (22). Associated with this evidence of a critical level are observations showing that the heart and parts of the brain are progressively damaged as the pressure is reduced and persists below that level.

If a hemorrhage is produced—for example, 15 or 20 per cent of the estimated blood volume—there is a sharp fall of blood pressure. Only a few minutes elapse, however, until the pressure is restored to approximately the former height. Thus a proper supply of blood is assured to the brain and to the heart. This remarkable and prompt adjustment of the circulation is a function of the sympatho-adrenal system, for in sympathectomized animals the rise after such hemorrhage does not occur (23). It results from proprioceptive reflexes, from the carotid sinus, and from the arch of the aorta, which operate in such fashion that the

blood vessels generally throughout the body, except in the heart and the brain, are contracted so that the capacity of the vascular system fits the reduced volume of blood and therefore maintains in these essential and most sensitive organs an adequate supply of oxygen.

We must conceive homeostasis, therefore, as involving not only the state of relative uniformity of the fluid matrix throughout the organism but also a local and specialized condition as manifest in active parts—muscles, for example—and in endocrine glands. Moreover, we must conceive the homeostatic mechanisms as being operated in such manner as to provide for preferential treatment of primarily important structures. Thus, in case of hemorrhage or the first stages of shock, a constant state is assured for the heart and the brain. This preferential treatment is obtained, to be sure, at the expense of other organs, organs in which the blood vessels are constricted and in which, therefore, the blood supply is temporarily reduced. Supporting the devices which provide local homeostasis there are the widely influential and well-recognized mechanisms. Thus, in vigorous exertion, when the laboring muscles are benefiting from local changes in the circulation, the heart, the blood vessels, the spleen, and the lungs are collaborating. By that collaboration they send to the muscles which are engaged in action a more abundant supply of oxygen and the material for effective performance, and they prevent in the organism as a whole an accumulation of waste arising therefrom. Also, after hemorrhage there is an inflow of fluid from the tissue spaces which increases the volume of the circulating blood. As this occurs there is gradual relaxation of the constricted blood vessels, and consequently a proper flow of blood to the organs which temporarily have surrendered their quota to the heart and brain.

Such are some of the newer aspects of homeostasis to which I call your attention. There has been no essential criticism hostile to the concept of homeostasis and no evidence which indicates that the sympathetic system does not play an important rôle in homeostatic regulation. Finally, there is recognition of the fact that we need much more information than we now have in order to understand more thoroughly the nice devices in the organism for maintaining its stability.

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THE WILLIAM HENRY WELCH LECTURES

II. HOMEOSTASIS IN SENESENCE¹

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The remark has been made that there is one organism always with us, concerning which we know very little, and that is the old man. The old man, of course, is not wholly unknown because some features of age are obvious. For example, the changes in the skin and its appendages in old age are especially striking. As men grow older many of them bear what Shakespeare called "the silver livery of age." The hairs not only turn white, they also grow long, in the ears, in the nostrils, and on the eyebrows. The nails become brittle, rigid, and discolored. The skin loses its elastic tissue so that when pinched up on the back of the hand it does not quickly snap back into place. Brown spots are likely to appear on the exposed parts of the body and there may be other changes of cutaneous pigmentation.

Furthermore, there are alterations in the sense organs. Hearing becomes less acute. We suffer as we grow older from what the aurists call "high-toned deafness," which does not mean what it might, but instead an inability to hear high tones. The high range of audition in youth, between 15,000 and 20,000 vibrations a second, moves gradually downwards in the later years until, in my own case, it is now about 9,000. There is a Dorsetshire proverb that no workman over 40 hears a bat squeak. The eyes likewise undergo changes in the late years. The near point for clear vision usually recedes so that without glasses we hold an object farther and farther away in order to have it in focus, and thereby we encounter the difficulty of too small and too dim an image on the retina. The conflict between these two difficulties introduces us to what Oliver Wendell Holmes called the "trombone age."

There is also a growing tendency toward inactivity. This is a very general phenomenon. One has only to compare the frolics of a puppy or a young dog with the slow movements and the somnolence of an old dog in order to have a striking illustration. Our own motions become gradually slower as we grow old, and we have less concern with sports and other outdoor activity.

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The problems presented by the aged are sure to become more and more urgent. Old persons are rapidly increasing in numbers. In 1911-12, millions of industrial policy holders of the Metropolitan Life Insurance Company had at birth a calculated life expectancy of about 46 years. In the 25-year period between 1912 and 1937 the figure had risen to 60 years; that is, the life expectancy had increased about 33 per cent (1). The mortality of industrial workers is higher than that of the general population. In 1935 the life expectancy of our general population at birth was over 61 years. The vital statistics of England tell the same tale in a different way. The percentage of persons above 60 years of age in the population of England, in 1901, was 7.4; in 1931 it had risen to 11.5, and in 1937 to 13. Here is an increase in the number of persons over 60 amounting to 75 per cent between 1901 and 1937. E. B. Wilson has estimated roughly that with continuance of the present fertility and mortality rates in the United States we may reasonably look for a distribution of age groups by 1975 about as follows: 30 per cent under 20 years of age; 50 per cent between 20 and 60; and 20 per cent, 60 years old or older. On the basis of that calculation we might expect to have 30,000,000 people over the age 60.

New problems are sure to arise with these changes of age distribution. The burden of old-age benefits will increase. The reserves for old-age security will have to be amplified. More accommodations for the senile, the blind and the bedridden must be provided. Associated with these extra demands there may be fewer accommodations for children—a lessened expenditure for child welfare, for schools, and for hospitals for infectious diseases. Perhaps as these alterations occur there may be greater attention to geriatrics and less to pediatrics.

Impressed by the importance of problems presented by greater numbers of aged persons and also by ignorance of the processes which are occurring in the senescent organism, the officers of the Josiah Macy, Jr. Foundation called a conference in June, 1937, to consider a scientific approach to the problems of the aging process. The members of the conference—physiologists, biochemists and zoölogists—were organized to make inquiries into what is known and what remains to be learned. The topic assigned to me was the aging of homeostatic mechanisms. On this occasion I wish to speak of the three homeostatic conditions about which most is known—the uniformities of temperature, blood sugar, and the acid-base balance in our bodies as we grow old.

Homeostasis of Body Temperature. Temperature homeostasis, as is well known, is the result of regulating continuous processes, the processes of heat production and heat loss. A fact of primary importance is that the internal temperature of elderly persons is usually kept within the normal range. Observations made on 185 individuals, ranging in age from 60 to 100, has revealed no alteration of body temperature as the

years increase. Though it is thus maintained, are the factors which maintain it undisturbed in the course of growing old? This is the central question.

Fundamentally heat is produced by the processes of chemical change taking place in the organism. The common measure of these processes is the basal metabolic rate. Various observers from the time of Magnus-Levy and Falk (2) in 1899 have testified that the speed of metabolism becomes gradually less with advancing years. The greatest accumulation of pertinent data on this point was gathered by Boothby (3) and his collaborators at the Mayo Clinic. They reported tests on 639 male and 828 female human subjects. The average figure for men at age 20 was 41.6 calories per square meter per hour. At age 40 it had fallen to 38.3 and at age 60 to 35.7—a drop of about 14.5 per cent from age 20. Studies by Matson and Hitchcock (4) and also by Benedict (5), on men whose ages ranged from 74 to about 90, revealed an average basal metabolic rate of about 30 calories per square meter per hour. This represents a fall of about 28 per cent from age 20. In round numbers we may expect that in late senescence the basal heat producing processes in the body will be reduced about 25 per cent, as compared with late years of early manhood.

The reasons for the reduced rate of heat production as we grow older are probably various. Pertinent among them are, first, indications of partial involution of the thyroid gland. In the thyroid glands of the aged have been found clusters of small follicles with little colloid in them; other clusters of follicles are much distended with colloid (6). Also there is a gradual increase of fibrous tissue, with lymphoid infiltration. The great importance of the thyroid as an agent maintaining normal heat production renders these observations significant. Another reason for a lowered metabolic rate may be muscular weakness and associated reduction of muscular vigor. Quetelet (7) tested the ability of persons of various ages to lift heavy weights. He found that this ability was approximately 40 per cent less at age 60 than it was between ages 25 and 35. Whether there is an associated reduction in muscular tone and therefore a reduced output of heat is not definitely known.

The explanation of a lessened heat production as one grows older is admittedly unsatisfactory. There remains, however, the fact that it is a limiting condition in the homeostasis of body temperature. The gradual decrease in the rate of combustion in old age still leaves enough heat produced to maintain normal temperature in ordinary circumstances. On exposure to cold, however, the slower burning in the body must be compensated for by putting on more clothing than is required in youth or middle age and by seeking a place near the stove or an open fire, or some other source of heat.

Besides a lessened ability to adapt to cold there is often in the aged a

lessened ability to adapt to external heat. It has been pointed out that this deficiency is more marked in persons with the *habitus corporis senilis luxus* than in persons with the *habitus strictus*. Sweating and vascular dilation may both be defective because, as mentioned earlier, the skin commonly undergoes atrophy in old age. A partial disappearance of dermal capillaries may occur, with concurrent degenerative changes in collagen and in elastic tissue. Furthermore, there is likely to be partial degeneration of sweat and sebaceous glands so that the skin becomes dry and rough in the later years of life. Also, with advancing age the intima of the arterioles may thicken, and there may be fibrosis of the media; in consequence of these changes the possibility of vasodilation of these blood vessels is reduced, and therefore the possibilities of heat loss by vasodilation are correspondingly reduced.

Pickering (8) has studied the maximal heat elimination from the hand when it was exposed to a standard amount of water at standard temperature. He found that the output of heat in calories per minute per unit volume of hand was 33 per cent lower at 70 years of age than at 25. These observations are quite in accord with the changes in skin and blood vessels which we have just surveyed.

Concordant with this evidence of lessened ability to get rid of body heat, or to adjust to increased temperature, is the evidence of an increased death rate from "heat stroke" in the later decades. The rate rises slightly after 60, and then goes up with striking rapidity. The figures for Massachusetts between 1900 and 1930 showed a death rate from heat stroke of 8 per 100,000 between the ages of 70 and 79; 20 between 80 and 89; and 80 between 90 and 100. Similar figures have been reported for the states of New York and Pennsylvania.

In reviewing the facts we have considered in relation to the homeostatic devices concerned with the regulation of body temperature, note that the powers of adjustment to high and low external temperatures are greatly restricted as one grows older. The homeostatic mechanisms are less and less able to adapt the organism to temperature variations in the external environment as age progresses in the later decades.

Homeostasis of Blood Sugar. We turn now to a consideration of the homeostasis of blood sugar. This is achieved by storage in the form of glycogen in times of plenty, by overflow through the kidneys when there is excess of glucose in the blood, and by release of storage in times of need. As is well known, the efficacy of the mechanisms for storage and for use of glucose in the body is measured by the so-called "glucose-tolerance test." After a standard solution of glucose is taken on an empty stomach the concentration of sugar in the blood is determined at intervals of a half hour, usually for about two hours. Normally there is a sharp rise in the concentration during the first half-hour to 160 or 170 mgm. per cent and thereafter a gradual return to the previous level in about two hours. When

the mechanisms are defective the resultant curve, indicating the conditions in the blood, is higher and longer than the normal.

Various observers have noted that in the later decades of life the test reveals a higher and more prolonged rise in the glycemic concentration than is characteristic of the earlier decades. The largest number of cases has been reported by John (9), who made the test on 192 children and 1500 adults. He found that the "diabetic" type of curve—a high and prolonged hyperglycemia, typical of diabetes—was found in only 10 per cent of individuals between 30 and 40 years of age, and that there was a gradual increase to 50 per cent between ages 60 and 70. Eighty per cent of the children had normal curves for glucose tolerance, whereas only 62 per cent of the adults were in this class.

These data indicate that with advancing years the human organism is prone to an impaired ability to use and store glucose at the rate characteristic of youth and early adulthood. Again we note that the homeostatic mechanisms become limited as we grow older. Unfortunately present ignorance of all the factors involved in regulation of the glycemic level does not allow us to state definitely what factors may be defective.

Homeostasis of the Acid-base Balance. We come finally to the homeostasis of the acid-base balance in old age. The chief homeostatic agents preserving the slightly alkaline reaction of the blood are the lungs, the heart, and the blood vessels. May I remind you that strenuous muscular activity—for example, a vigorous struggle—is associated with a large production of lactic acid. Unless this non-volatile acid is promptly burned to volatile carbonic acid, it will overwhelm the alkaline buffers in the blood; these are the first defenses of the organism against the development of an acid reaction which, even when slight, is highly dangerous. The burning of lactic acid requires an abundance of oxygen in the active tissues. This is provided by an increased depth and rate of respiration, by a rise of general arterial pressure with dilation of the blood vessels in the active parts, and by increase in the volume output of blood from the heart per beat, and also per minute because of faster rate. The consequence of these vascular changes is a greatly increased use of the carriers of the respiratory gases between the tissues and the lungs—oxygen to the tissues and carbon dioxide to the lungs. The questions, then, which are before us are the changes in the homeostatic mechanisms concerned with the avoidance of accumulation of acid in the blood as age advances.

The first change which we may note is a lessening of the capacity for ventilation of the lungs. Nearly one hundred years ago Hutchinson (10) reported on the maximal to-and-fro movement of respired air (i.e., the vital capacity) in 1,775 healthy cases. He found that there was a gradual diminution of the vital capacity from a maximum between 30 and 35, until in the period between 60 and 65 it was only 80 per cent of the earlier figure. The normal vital capacity of young adults, as determined by a

large number of cases, was found to be approximately 3,750 cc. for males and 2,600 cc. for females (11). In an examination of 110 men between 60 and 94, and 71 women with approximately the same range of ages, Levy (12) confirmed Hutchinson's figures for the period 60-65 and discovered that in the late 80's the average vital capacity of males was reduced to 2,350, a fall of 37 per cent, and in females to 1,460, a fall of 43 per cent from the averages for young adults. It might be supposed that the vital capacity, as measuring a maximal effort, might fall without a corresponding fall in the ordinary physiological capacity of the lungs. It appears to be true, however, that as the vital capacity is reduced in old age the pulmonary ventilation in maximal muscular work is similarly reduced. Recent studies by Dill and Robinson (13) have disclosed that in elderly men the respiratory movements in supreme exertion are reduced to a degree corresponding to the diminished vital capacity, or to even a greater degree.

The lessened mobility of the thoracic wall may be attributed to a weakness of the intercostal and other respiratory muscles which may result from lack of exercise or the indolent habits of the aged. It may be attributed also, and perhaps more reasonably, to a stiffening of the attachments of the ribs. Determinations of the calcium content of the costal cartilages have shown that whereas it amounts to 125 mgm. per cent of dry substance in youth, it rises to 617 mgm. per cent in the fifth decade and to approximately 1,400 mgm. per cent in the seventh decade (14). The accumulation of lime salts in the flexible attachments of the ribs may result in such rigidity that a deep intake and vigorous output of air, possible in earlier years, become impossible as one grows older.

Vascular changes occurring in senescence likewise induce limitations. First, the arterial pressure commonly rises as men and women pass into and beyond the decade of 30 to 40 years. Blood-pressure measurements are more highly variable than other measurements because methods vary and disturbing conditions are likely to appear which are not always controlled. In a statistical study of 4,000 cases Saller (15) found a gradual rise of the average systolic arterial pressure (with little change in the diastolic pressure) in the later years. According to Saller's results the arterial pressures in men between 21 and 47 years of age were 144 systolic and 98 diastolic; between ages 68 and 89 these figures rose to 186 systolic and 86 diastolic. Similar changes occurred in women in the same age groups, but in general the figures were higher than for men. Although these statistical data are more extreme than have been reported by other observers, they agree with other data in showing the tendency of the systolic arterial pressure to rise as the decades pass.

Another change which is probably associated with the increased blood pressure is a diminishing elasticity of the arteries with advancing years. The elasticity has been estimated by determining the velocity of the pulse

wave. Bramwell, Hill and McSwiney (16) measured the velocity of the wave in 74 individuals between 5 and 84 years of age. The elasticity was expressed as 47 per cent at 5 years; it was found to be reduced to 17 per cent at 80 years. Hallock (17), using a more delicate method for registering the pulse wave and studying 400 persons with ages ranging from 5 to 65 years, found a close correspondence with the results reported by the earlier observers up to age 45, and thereafter a more rapid loss of elasticity than in the smaller group. Obviously, if the arteries are more rigid everywhere in the body and not merely in the superficial samples taken for examination, they could expand less in the active muscles of the old than in the young.

There is evidence that capillaries, as well as arteries, may have impaired functions as the years pass. Histological examination of muscles has revealed that there is a laying down of interstitial colloid in old persons and a thickening of the elastic tissue which surrounds the muscle fibers (18). In this interfibrillar region lie the capillaries. If this extra material is interposed between them and the muscle cells it is obvious that the capillaries, even should they dilate when the muscle becomes active, could not perform their function satisfactorily, for the diffusion of the respiratory gases especially oxygen, which has a relatively slow diffusion rate—would meet with obstruction.

The third homeostatic factor which has been mentioned is the heart. Observations on cardiac performance in senescence have shown that that organ does not meet the demands in later, so well as in earlier, decades. Dill and Robinson (13) have made records of the cardiac rate of 91 boys and men ranging in age from 6 years to nearly 70. These subjects were required to run on a treadmill having a slope of 8.6 per cent. The speed of the treadmill varied according to the subjects' ability to run. It was sufficiently great, however, to render almost all of the subjects exhausted in three to five minutes. The mean of the maximal heart rate of nine boys, having an average age of about 14 years, was 196 beats per minute. In seven men with an average age of 63 years it was 165 beats per minute. The intervening ages showed a continuously downward trend in the ability of the heart to keep the faster pace as the years increase.

It seems probable that in the elderly the heart is not only beating at a less rapid rate but also with a reduced efficiency. The "hypodynamic heart" of the untrained person functions differently from the vigorous heart of the athlete. When the well-trained individual engages in vigorous exertion the heart not only beats somewhat more rapidly but also empties itself more completely of the blood delivered to it from the veins. The "hypodynamic heart" of the untrained person, on the other hand, meets the situation differently. It dilates and thereby has the physical advantage of greater length of muscle fibers, but it does not empty itself effectively, so that the increased output per minute depends largely on the

more rapid beat (19). This suggested difference between the young and old requires, however, further evidence before it can be accepted as reliable.

In surveying the homeostatic mechanisms concerned with protection against the development of an acid reaction in the blood—the lungs, the blood vessels, and the heart—we note that as life goes to its later stages there is a gradual narrowing of the capacity to adapt the needs of the organism to the special requirements presented in muscular effort. These mechanisms work satisfactorily in a routine, quiet existence, but stress, even relatively slight stress, may encroach sharply on the limitations.

What are the results of these limited capacities of the lungs, blood vessels, and heart? Mori (20) subjected youths and men, ranging in age from 17 to 57, to standard work for ten minutes on a bicycle ergometer. In four youths of the second decade the alkaline reserve of the blood was lessened to a degree indicated by a reduction of 4 volume per cent of CO_2 . In thirteen men of the fifth decade the reduction was 12 volume per cent CO_2 . It is probable that in these cases the lessened alkaline reserve was due to an increase of lactic acid coming from the laboring muscles. That inference is supported by observations made by Dill and Robinson. Their subjects walked on a treadmill having a slope of 8.6 per cent. A rate of walking of 3.5 miles per hour increased the metabolism until it was seven times the basal. Examination of the blood in the subjects showed that the lactic acid which was present was more than three times as much at age 60 as it was at age 20. Fortunately in these studies we have definite facts on which to base the explanation of the greater appearance of lactic acid in the older subjects. It should be emphasized that all subjects were performing fairly hard work. A measurement of the oxygen carried from the lungs per minute in these individuals was gradually less with advancing years. At age 17 it was 53 cc. per kgm. per minute, at age 35 it was 43 cc., and at age 63 it was 35 cc.—a drop of 34 per cent. These are figures which have their reasonable explanation in the lessened ability of lungs, blood vessels, and heart to meet the demands of vigorous effort as one grows older.

Concordant with the foregoing data is the evidence presented by records in competitive sports. The best times for the 100-yard dash have been made by youths or young men; the present record was first made by Wykoff at age 21. The records from one to five miles are held by men with ages ranging between 23 and 27 years. The record for ten miles was made by Nurmi when he was 31 years old. DeMar, who has run Marathon races since he was 22 years old and who is now 50, made his best showing between the ages 36 and 42. It appears that, as speed alone becomes less important for running, and judgment and endurance become more important, the records are held by older men.

Reports of the performance of baseball players and tennis champions likewise furnish evidence that the ability to mobilize quickly the bodily

forces is gradually lost after a peak at the period between 30 and 35 years of age. Experts have testified that after 35 years the professional players of baseball begin to "slow up," their "legs fail," they lose the speed they had earlier. There are few stars in sport after 40.

It is of interest to note that associated with the limitations of homeostatic mechanisms in advancing years there is, as Miles (21) has shown, a limitation of the rapidity of movement of hands and feet. In his experiments the subjects reached forward, picked up an object and placed it in a distant position, or they moved a foot in a required manner. These actions were performed at a rate which was gradually less and less after the fourth decade. Studies of men working on speed machines in great factories have shown that they likewise begin to find difficulty keeping the pace of the machine after about age 40. Indeed, they may suffer from what is known as a "speed-up neurosis," because they find they have difficulty in moving at the rate demanded by the machine, and yet must do so in order to keep their job. These are facts which must be recognized in industry as natural phenomena of the aging process.

In a final survey of the facts which we have considered we note that in temperature regulation, in the storage and use of sugar in the body, and in the maintenance of the acid-base balance of the blood the homeostatic mechanisms when subjected to stress are revealed to be more and more limited in their ability to preserve uniformity of the internal environment as life advances into the last decades.

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STRANGULATED HERNIA AND GANGRENOUS APPENDIX IN A PREMATURE INFANT

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This contribution is presented because it exemplifies how in an emergency one may be obliged to break the accepted rules of surgical procedure and in spite of this, succeed. Our dear friend, Alexis Moschcowitz, gone but still vivid in our memories, added much to surgery, especially to the permanent repair of hernia. He would surely have been interested in the report which follows.

The story of Richard T., published many years ago¹ is briefly repeated here with follow-up notes to the present time. The patient was born March 31, 1908, six weeks before the end of a carefully computed term of pregnancy. There had been three cases of appendicitis in the immediate family. A small reducible right inguinal tumor had been noted soon after birth and it gradually extended into the scrotum. At the age of three weeks and three days a truss with a small wooden pad was applied, the hernia having been apparently reduced. At once there was so much restlessness and pain that the appliance was removed in four hours; but in spite of this, the baby cried and ceased nursing after a few minutes. The ingested milk was regurgitated. Rather suddenly, next morning, there was a great change in the infant's expression; a hollow-eyed appearance, with a sinking of the fontanelle, slight cyanosis, and what looked like the beginning of a collapse. Although the greater part of the hernia could still be reduced, there was a slightly indurated mass in the scrotum, and there was edema of the prepuce. I saw this patient with Dr. Edward W. Perkins just a day after the application of the truss. In addition to the signs described, the abdomen was rigid and distended. Local physical examination produced straining and crying. The bowels had moved twice, and some gas had been expelled. While I was present, the child suddenly seemed moribund, but he revived after the stimulation of a little diluted brandy. The temperature was below 96°F. The urine was high-colored, so that it stained the linen. Evidently there was some form of strangulation, and in these desperate straits I decided that operation was the only thing which might save life.

The baby was taken to the Mount Sinai Hospital, and under general anesthesia—chloroform and ether—induced by the late Dr. Thomas L.

¹ J. A. M. A., Aug. 29, 1908.

Bennet, I made a final effort to reduce the bulging by taxis, but soon abandoned this and incised in the usual manner for herniotomy. The parts being so minute, it was necessary to use the smallest instruments available. The tiny mouse-tooth forceps of the ophthalmological armamentarium was employed. When the sac was opened a tense and distended coil of large intestine appeared.

Any effort at replacement without first dividing the neck of the sac would have endangered the integrity of the gut. With the freeing of the viscus there was a gush of three or four ounces of serous fluid, and then I was able to reduce the greater part of the hernia. The quantity of fluid was very great, when one realizes that the child weighed only about five pounds.

The appendix still lay within the scrotum and, on withdrawing it, I was surprised to find that its distal half was black and gangrenous. I crushed its root and mesentery and then firmly tied them with a single ligature, and ablated with scissors. It appeared that any attempt to do more than had already been accomplished would increase the operative shock, so what remained of the inguinal canal was packed with gauze which also filled the entire wound. A heavy starch bandage was applied, including the lower extremity in the extended position down to the foot, and this rigid dressing was reinforced with wooden splints. It should again be noted that no part of the wound was closed by suture. The total time of the operation was twenty minutes, and Richard was taken home immediately after its completion.

It interested me greatly to note that a culture from the interior of this gangrenous appendix revealed colon bacilli, although the child was so very young, and had been breast-fed throughout, with the exception of one or two occasions when he had tasted unboiled water. This examination was made in the pathological laboratory of the hospital by Dr. Abraham Sophian, now a physician of Kansas City, and the result was confirmed by other members of the Staff. This certainly is an instance of the pervasiveness of this bacterial organism.

There was uneventful recovery. The first change of dressing was six days postoperatively, and healing was complete two weeks following the herniotomy. Ten days after the operation the scales showed the amazing increase of about 40 per cent of the body weight, or two pounds.

The former patient is now thirty-one years old. There was a slight bulging of the groin when he was about twelve years of age, but it disappeared spontaneously. He is in perfect health, and has never worn a truss.

Some years after the operation described, I had a similar case which I saw with Dr. Henry Heiman. This child was eight days old, and during his struggles at the time of operation, there was almost complete evisceration. Seven years later there was no recurrence, but further than this the case was not followed.

It is my opinion that strangulated hernia in these very young babies should not be treated by plastic surgery. If one may judge by these two cases, the packing method gives promise of complete recovery. Should there be a recurrence at some future time, it may be treated according to the conditions found, probably by classical hernioplasty.

The cause of the gangrene of the appendix in the case of Richard T. must have been interference with the circulation by the truss pad.

SUMMARY

Presentation of a case of gangrenous appendicitis infected by colon bacilli, complicating a strangulated hernia in a premature child.

JEJUNOSTOMY FOR ALIMENTATION

A LIFE-SAVING PROCEDURE

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The following case report is presented not to stress the multiplicity of postoperative complications which may befall a patient or the ability of that patient to survive them, but to call attention to the life-saving procedure of jejunostomy performed for feeding purposes.

CASE REPORT

First Admission. August 9, 1933 to September 6, 1933.

History. (Adm. 378736). An unmarried Italian female, aged 16, was admitted to the Medical Service of The Mount Sinai Hospital complaining of abdominal pain and jaundice. Her past history included a tonsillectomy at the age of 5 years, questionable rheumatic fever at 13 years, and pneumonia at 15 years. There was no history of typhoid fever. Two weeks prior to admission she became ill with epigastric pain and vomiting which lasted four hours. These symptoms returned two days prior to admission, lasted several hours, and left a residual soreness in the right upper quadrant. Fever and jaundice were first noted on the day of admission.

Examination. The temperature was 100.2°F.; pulse 120 per minute. Faint icterus was present. The liver was enlarged and the spleen was just palpable. There was slight upper abdominal tenderness.

Laboratory data. Hemoglobin was 70 per cent, red blood corpuscles, 4,390,000; white blood corpuscles, 5,200; polymorphonuclear leucocytes, 70 per cent; lymphocytes, 25 per cent; monocytes, 5 per cent. The urine was negative. The blood Wassermann test was negative. The blood chemistry was as follows: urea nitrogen, 12 mg. per 100 c.c.; sugar, 85 mg. per 100 c.c.; total cholesterol, 200; cholesterol ester, 55; Van den Bergh: direct negative, indirect 1 250,000, 0.4 mg.; icteric index, 17. An X-ray examination of the abdomen failed to reveal any radiopaque gallstones. The galactose tolerance test was normal.

Course. A diagnosis of catarrhal icterus (toxic hepatitis) was made and this seemed to be substantiated by the subsequent course. The jaundice and abdominal tenderness disappeared, the liver became smaller, and the cholesterol ester was consistently low in proportion to the total cholesterol until the time of discharge when normal figures were obtained.

During her hospital stay, the patient had several attacks of generalized tonus with carpal spasm but no pedal spasm. The blood calcium was normal. These attacks were thought to be hysterical in origin.

Following her discharge from the hospital, the patient was well, except for rare similar attacks of generalized tonus, until one and a half years later when she had an attack of mid-epigastric pain which radiated after a time to the right upper quadrant and right infra-scapular region, and was accompanied by vomiting. On the third day of her illness, jaundice was noticed. The following day she experienced a shaking chill lasting fifteen minutes associated with a temperature rise to 103°F. She was admitted to the hospital several hours later.

Second admission. April 14, 1935 to June 13, 1935.

Examination. The patient was an acutely ill, thin female of 18 who was very slightly icteric. The temperature was 102.6°F. and the pulse 108 per minute. There was definite tenderness and slight spasticity in the epigastrium and the right upper quadrant of the abdomen. The liver and spleen were not palpable.

Laboratory data. The blood count revealed:—white blood corpuscles, 13,800; polymorphonuclear leucocytes, 70 per cent; lymphocytes, 20 per cent; monocytes, 10 per cent. The urine contained bile and a trace of urobilin. The stools were brown in color and otherwise normal.

Operation. The preoperative diagnosis was acute cholecystitis, cholelithiasis, and possibly choledocholithiasis. Laparotomy was performed (G.D.O.) on April 16, 1935, under gas, oxygen, and ether anesthesia. The appendix was removed. The gallbladder was then inspected and found to be moderately thickened and injected. No stones could be palpated in the gallbladder or the common duct. The gallbladder was removed subserously from above downwards. The common duct was inspected, found to be dilated, and was opened. About forty small stones were removed with a small blunt curette. When all had seemingly been removed, a probe was passed into the duodenum without encountering any obstruction. A straight tube with multiple side holes was placed into the common duct pointing upwards and the common duct was closed about it. A packing was apposed to the raw liver bed, a tube was inserted into Morrison's pouch, a rubber dam was placed about the other drains and the abdomen was closed in layers.

The gallbladder was subacutely and chronically inflamed and contained three facettted stones. The choledochal stones were round, about 2 mm. in size, and appeared to be composed of almost pure bilirubin.

Postoperative course. The patient's temperature rose sharply to 104.4°F. within the first eighteen hours. She vomited moderate amounts of green and brown fluid. The choledochostomy tube drained several ounces of clear bile daily. On the third day, the abdomen which had been moderately distended, became more distended, especially in the lower quadrants.

The temperature had dropped to 100°F. Despite a fair urinary output and a moderate amount of intravenous fluids, the patient's tongue remained dry and her blood chemistry studies revealed a urea nitrogen of 62 mg. per 100 c.c. and chlorides of 410 mg. per 100 c.c. Vomiting of yellow-green fluid continued. Enemata and colonic irrigations, although returning both stool and flatus, failed to relieve the rapidly increasing distension. Intravenous fluids were continued and a Levin tube was passed. Only ten ounces of gray, sour-smelling fluid were obtained. On the fourth postoperative day, the patient's condition seemed definitely worse. The vomiting continued. The lower abdominal distension became enormous, although the upper abdomen was only moderately distended. Bladder retention was suspected, but catheterization disproved this. An X-ray picture, taken to determine the presence or absence of intestinal obstruction, disclosed a large mass filling almost the entire abdomen. In the pelvis, there were loops of small intestine which were not dilated but which contained gas. The colon was displaced laterally and contained a small amount of gas.

Blood chemistry studies at this time revealed a marked alkalosis, the carbon dioxide combining power being 73.5 volumes per cent (presumably due to the loss of chlorides in the vomitus).

A Levin tube was again passed and 4,200 c.c. of sour-smelling fluid and much gas were obtained. No bile was present in this fluid. The distension was immediately and markedly relieved.

The following morning the patient was again distended and the passage of a Levin tube resulted in the evacuation of 1,250 c.c. of sour-smelling gray gastric contents, no bile being present. The patient continued to be quite sick, her temperature ranging from 101° to 105°F.

During the next several days, an indwelling Levin tube drained everything taken orally. Mineral oil and insoluble carmine which were given by mouth failed to appear in the stools but were completely recovered in the Levin tube drainage. Although the Levin tube was clamped off for long periods of time, nothing passed through the stomach.

The patient began to show very slight improvement in her general condition but then suffered several serious setbacks. A bilateral suppurative parotitis appeared. The left side ruptured into the external auditory canal, but despite this and multiple bistoury incisions it was nevertheless incompletely drained and later required several liberal incisions. The right side appeared to be slowly subsiding. On the tenth postoperative day, the patient's wound disrupted. This complication was treated by packing the wound with iodoform gauze and strapping it with adhesive. Definite signs of pneumonia developed in the left lower lobe. The patient's temperature ranged between 102° and 105.6°F.; her pulse varied from 128 to 140 per minute. She continued to go down-hill, and developed a toxic exhaustion psychosis.

After the fifth postoperative day, large doses of atropine were repeatedly given by hypodermic injection in order to overcome any pylorospasm, if such was the cause of the gastric retention. After the complete gastric obstruction had been present for two weeks, there was some slight temporary patency of the pylorus indicated by the fact that mineral oil, given by mouth, was subsequently found in the stool on one occasion. However, the drainage by Levin tube continued to be greater than the intake by mouth. The external biliary drainage was about 12 ounces daily. The stools contained bile. Despite two transfusions of citrated blood the patient became more and more anemic. Adequate glucose, fluids, and chlorides were administered by venoclysis but the patient continued to have a severe alkalosis (blood carbon dioxide combining power—71 volumes per cent) and became progressively more asthenic and emaciated.

On the sixteenth postoperative day, barium was given by mouth and X-ray observations were made at one, two, seven, and twenty-four hours after ingestion. All the barium remained in the stomach. None was seen in the rest of the alimentary tract at any of the observations.

It now became apparent that although the patient was receiving all forms of parenteral supportive and nutritive therapy, a fatal outcome was shortly to be expected. Because of the progressive emaciation, weakness, anemia, and continuous loss of gastric secretion leading to alkalosis, one could not wait longer hoping for spontaneous alleviation of the evident pyloric obstruction. Some form of enteral feeding had to be instituted. To attempt to find and relieve the cause of the obstruction through the infected previous operative field in this weak, toxic, and rapidly failing patient was considered foolhardy. Gastroenterostomy was considered but was not performed because of the experience that large dilated atonic stomachs do not function properly after this procedure. The simplest and most direct method for alimentation was deemed to be feeding via the jejunum and, accordingly, on the seventeenth postoperative day, a Witzel jejunostomy was performed (G.D.O.) under local anesthesia, at a point eight inches below the ligament of Treitz.

Feedings through the jejunostomy tube were started eight hours after operation. Water, peptonized milk, orange juice, bile salts, viosterol, and the Levin tube drainage (gastric contents) were given by slow gravity drip. Later, the Scott-Ivy pabulum (1) as used by Wolfer (2) was employed. Slight colic but no diarrhea followed.

Two days after the above operation, several abscesses in the right parotid gland were incised and drained.

On the twenty-first day after the original operation, bile was found in the gastric contents indicating a patency of the pylorus. The inability of the stomach to empty itself, however, was further demonstrated by the finding of moderate amounts of barium in the stomach on repeated lavages.

The patient began to improve. The jejunal feedings were increased

until the patient developed a mild diarrhea. She continued to run temperatures between 101° and 104°F. but the daily improvement in her general condition was remarkable. One week after the jejunostomy, the indwelling Levin tube was removed. Small feedings were given by mouth, in addition to the jejunal feedings, and the stomach was washed out twice daily. At first only very small quantities passed through the pylorus. The amounts however increased slowly so that on the thirty-ninth day after the original operation and twenty-two days after the institution of the jejunostomy, ingested food began to go through the pylorus in quantities up to fifty ounces daily without any gastric retention. The jejunostomy feedings were nevertheless continued in order to force nourishment. The patient's condition improved rapidly. The temperature slowly dropped to normal. Gastric retention did not recur. The parotid and abdominal incisions began to heal more rapidly and the biliary fistula closed. The jejunostomy tube was clamped off and adequate nourishment was given by mouth. On the fiftieth postoperative day (thirty-three days after jejunostomy), the patient was allowed out of bed. Four days later the jejunostomy tube was removed and the jejunostomy wound promptly closed. The patient was discharged from the hospital shortly thereafter.

The patient has been observed in the Follow-Up Clinic. At her last visit on October 16, 1937, she was in good health despite a moderate-sized, right upper quadrant incisional hernia.

Comment. There are several interesting features concerning this case which should be briefly noted. The occurrence of gallbladder disease and particularly common duct stones in a young unmarried female of 16 is decidedly uncommon. Catarrhal jaundice was the diagnosis originally entertained on her first admission but the cause was indubitably partial obstruction by the many tiny common duct stones. The extreme gastric dilatation which was present caused such enormous lower abdominal distension as to simulate bladder retention. In this case, the limits of gastric distensibility, as proved by experiments on cadavers (3, 4), was reached, namely between four and five liters. The etiology of the pyloric obstruction is a matter for speculation. It may have been due to pylorospasm, or gastric atony subsequent to acute postoperative gastric dilatation or to an inflammatory reaction or exudate from the contiguous operative site. The completeness of the obstruction led to a continuous loss of gastric secretion with subsequent alkalosis of a moderately severe degree. The obstruction lasted approximately thirty-nine days, after which spontaneous subsidence occurred.

The institution of enteral feeding through the jejunostomy tube was undoubtedly a life-saving procedure in this case. Parenteral administration of fluids, saline, glucose, and blood had not been sufficient to maintain the patient suffering from so many postoperative complications. The

clinical improvement following jejunostomy and forced jejunal alimentation was indeed dramatic. By this method, much needed foods, including protein, mineral elements, vitamins, and the patient's own gastric secretions, were given in large quantities. The patient's general condition started to improve almost immediately and excellent nutrition was maintained for a period of twenty-two days after which time patency of the pylorus and passage of food through it was reestablished.

Jejunostomy for feeding purposes was performed as early as 1885 (5). Since that time, many contributions to this subject have appeared. Diarrhea and severe enteritis followed jejunal alimentation in experimental dogs. In 1931, Scott and Ivy (1) described a non-irritating method and pabulum by which they were able to avoid these complications and maintain life for an indefinite period. Scott, Holinger and Ivy (6) kept a dog alive and well during a sixteen week period by this method, even though there was a complete loss of gastric juice. Their results have been applied clinically in a wide variety of cases with great success (2). The varied indications for jejunostomy for alimentation and other purposes in humans have been described by Heyd (7) and Wolfer (2). The operative procedure is simple in technic, can be performed quickly and under local anesthesia. Wesson (8) recently reported seven cases of long continued postoperative gastric retention following operations upon the stomach treated by jejunostomy without mortality from this procedure.

SUMMARY

Jejunal alimentation may be used in a great variety of conditions. Its value in the unusual case herein described cannot be over-emphasized.

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INHIBITION OF FUNCTION IN ONE KIDNEY DUE TO HYDRONEPHROSIS SECONDARY TO URETERAL OBSTRUCTION FROM OVARIAN TUMOR

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Clinical and experimental evidence has shown that a kidney will atrophy very rapidly after complete occlusion of the ureter. In the rabbit this occurs in about three months. Inhibition of function of one or both kidneys, due to pressure from large pelvic tumors, thus necessitates early removal of the tumor. This indication may be overlooked unless intravenous pyelography and cystoscopy are done.

CASE REPORT

History (Adm. 417319). The case presented is that of a 30 year old woman, married fourteen years, gravida 0, para 0. Her past history was marked by measles, diphtheria, an appendectomy at the age of 9, and the drainage of an ischiorectal abscess seven years previously. Her Wassermann test had been positive for ten years, although she had had antiluetic treatment intermittently. She entered the hospital on December 1, 1937 because of dull intermittent lower abdominal pain and backache for five days, accompanied by frequency and urgency of urination. Her menstrual history had been regular, occurring every twenty-one days and lasting for four to five days, until six months ago. During the six months preceding her admission the menstruation occurred at two week intervals and was very profuse.

Examination. Except for the presence of a large pelvic and abdominal tumor, the general physical findings were essentially negative.

The pelvic examination revealed a large cystic mass occupying the entire lower abdomen and reaching to halfway between the umbilicus and xiphoid. The uterine body appeared to be sinistroverted, unenlarged, and limited in its motility.

Laboratory Data. The sedimentation time was 22 minutes; the hemoglobin 62 per cent: The Wassermann test was 4 plus, and the blood pressure was 118 systolic and 82 diastolic.

Course. Because of the size of the pelvic tumor intravenous urography was done, in accordance with the usual practice on the gynecological service. This showed a normal upper urinary tract on the left side and no visualization of the kidney or ureter on the right. The urinary bladder

was pushed down, due to pressure from a mass extending upwards to the third lumbar vertebra.



FIG. 1. Intravenous pyelogram showing normal left urinary tract and no visualization of the right urinary tract.



FIG. 2. Retrograde pyelogram showing site of obstruction due to kinking in the right ureter, hydro-ureter, and hydronephrosis. The outline of the pelvic tumor can also be seen.

A cystoscopy was done simultaneously with an intravenous injection of indigo carmine. The left ureter was easily catheterized for 25 cm. and

there was a good excretion of indigo carmine after three minutes. The right ureteral orifice was difficult to visualize, due to its displacement. There was no dye or urine excreted from the right ureter. There was an impassable obstruction to a ureter catheter at 2 cm. A Woodruff catheter was inserted for the same distance and, under pressure, 30 c.c. of hippuran was injected and an X-ray picture taken. This showed kinking of the ureter at the point where the obstruction to the catheter was encountered. The ureter and kidney showed hydro-ureter and hydronephrosis.

A Rubin test was also performed because of the patient's history of sterility. This test showed that both tubes were closed.

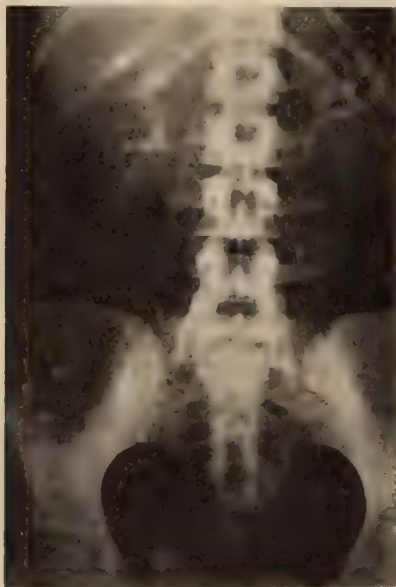


FIG. 3. Intravenous pyelogram following removal of the right ovarian cyst showing normal visualization of both kidneys.

Operation. A large unilocular cyst was found to occupy the entire pelvis and abdomen. It extended between the layers of the broad ligament, the meso-sigmoid and was adherent to the posterior surface of the uterus. There was a hydro-salpinx in the right tube. The left ovary was normal, but adjacent to it were two parovarian cysts, the larger one measuring $1\frac{1}{2}$ inches in diameter. The left tube was also the site of a hydro-salpinx. A right salpingo-oophorectomy was performed after three litres of sero-sanguineous fluid were aspirated. The parovarian cysts were removed and the clubbed end of the left tube was resected, leaving about $1\frac{1}{2}$ inches of the proximal part of the Fallopian tube. The pathological report was unilocular hemorrhagic cyst of the ovary measuring 25 by 12 cm.

Postoperative Course. The patient's convalescence was uneventful, her temperature never rose above 100°F. after the third postoperative day. An intravenous pyelogram done twelve days after the operation revealed a normal upper urinary tract on both sides; the right kidney pelvis was slightly larger than the left, but both kidneys appeared to be normal in size, shape, and position. A Rubin test, done fifteen days after operation, revealed patency of the stump of the remaining left tube. The patient was discharged, well, on the fifteenth postoperative day.

Comment. One of the interesting features in this case is that the inhibition of the function of the right kidney produced slight symptoms and was entirely obscured by the presence of a large ovarian tumor. This was probably due to the fact that the inhibition of the kidney function was gradual and that the pyelovenous and tubulovenous backflow was able to prevent overdistension of the kidney pelvis. When this mechanism becomes incompetent, complete anuria and atrophy of the kidney results.

SUMMARY

A case is presented with inhibition of the function of one kidney which was cured by the removal of a large ovarian cyst. It was also interesting to note that patency could be demonstrated in part of one tube following the resection of the diseased portion. The luetic infection is under treatment.

BLEEDING MECKEL'S DIVERTICULUM IN A TEN MONTHS' OLD INFANT

SAMUEL B. WEINER, M.D. AND GABRIEL P. SELEY, M.D.

[From the Pediatric Service of Dr. Bela Schick and the Surgical Service of Dr. Ralph Colp]

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CASE REPORT

History (Adm. 403634). A female white infant, 10 months old, was admitted to the Pediatric Service on January 18, 1937. For two days prior to admission she had passed bloody stools. Her illness began January 13 with a mild upper respiratory infection which lasted two days. On the following morning the child vomited once and shortly thereafter passed a bloody stool. This stool was well-formed, contained a moderate amount of fresh, bright red blood, no mucus, and no pus. During that day the child had two more stools of similar character. There was no apparent abdominal pain or discomfort, and no colic. The bloody stools continued for the next two days—two being passed daily. Marked pallor developed during this time.

The child was born one month prematurely and weighed 2070 gm. She was kept in an incubator for six weeks and did well. Following this her diet and development were both normal and adequate. Only after very close questioning, was the fact elicited that at five months of age the child passed a stool with a small amount of bright red blood in it. Because there were no associated symptoms and no repetition of the melena, the mother did not even report it to the pediatrician who was caring for the child. No family history of any hemorrhagic tendency was obtained.

Examination. On admission the child was pale, well-developed and well-nourished. She was in no distress and did not seem to have any pain. No purpura or eruptions were present. There was moderate generalized glandular adenopathy. There were no abnormalities in the pharynx or chest. The abdomen was full, but not distended. There was no fluid wave, no localized rigidity or tenderness. No masses were palpable. There was a sensation of fulness in the right lower quadrant. Rectal examination showed the same sense of fulness in the right lower quadrant. No masses were felt. On examination, black clots of blood without mucus were present. Proctoscopic examination (by the referring physician) showed no abnormalities.

Laboratory Data. The hemoglobin on admission was 45 per cent (7.5 gm.). Blood count: red blood cells, 3,900,000; white blood cells, 7,400;

platelets, 146,000; polymorphonuclear cells, 23 per cent; mononuclear cells, 79 per cent. Bleeding time, 3 minutes. Urine, negative except for the presence of 10 white blood cells per high power microscopic field.

Course. The diagnosis entertained on admission was bleeding Meckel's diverticulum, principally because of the history of previous melena, marked blood loss, absence of colic and inability to palpate an abdominal mass.

An immediate transfusion of 175 c.c. of citrated blood was given with marked improvement in the child's general condition. The child continued to have two to three stools daily with small amounts of blood in them. A gastrointestinal X-ray series was done but this showed no definite abnormality. Proctoscopic examination was repeated and showed no ulceration or polyps. The blood seemed to be coming from a point high in the intestinal tract.

Operation. On January 23, 1937, after a second transfusion, exploratory laparotomy was done by Dr. R. Colp. Under avertin-ether anesthesia



A. External view of the specimen.

B. Internal view of the specimen, showing the ulcer.

the abdomen was opened using a right rectus muscle-splitting incision. About 32 cm. from the ileo-cecal valve, an inflamed Meckel's diverticulum was found adherent to the mesentery of the terminal ileum. It measured 2.5×3.5 cm. and its base arose from the anti-mesenteric border of the ileum. The diverticulum was excised, the base being ligated with a heavy silk suture. After careful carbolization, the base was inverted by a purse-string suture. The abdomen was closed with heavy silk through-and-through sutures. No drainage was employed.

The postoperative course was uneventful. Parenteral fluids were given for forty-eight hours by continuous intravenous drip. There was no gastric retention. Dilute milk feedings in small quantities were begun after twelve hours and were rapidly increased to basal levels. Two days after the operation the child had a spontaneous normal bowel movement. The incision healed by primary union and on the eighth day the pincettes were removed. On the twelfth day the sutures were removed. The

stool was entirely normal after operation. On the sixteenth day the child was discharged in excellent condition on a full diet.

The following is the pathological report of the surgical specimen by Dr. Paul Klemperer:

"Specimen consists of a resected Meckel's diverticulum received unopened, 2 cm. in length. The serosal surface is smooth and glistening except for one point where there are a few fibrous adhesions covering an area of 0.5 cm. In the center of this area there is a slight depression and the underlying tissue at this point feels indurated. This area lies midway between the line of resection and the tip. The mucosa at the line of resection bulges out from the lumen and appears grayish pink and finely granular. When the diverticulum is opened longitudinally, the mucosa is seen to be composed of two types. The distal half appears grayish, rather high and velvety, definitely rugated and resembles gastric mucosa. The mucosa of the distal half is, as described above, pinkish gray and finely granular. In this portion a small ulcer is discovered.

"It is roughly oval in shape and measures 5 mm. in its transverse diameter and 3 mm. in its longitudinal diameter. The ulceration extends down apparently to the muscularis mucosa. The edges of the ulcer are rounded and the base is grayish. This ulcer is situated immediately opposite the depressed area described above the serosa.

"*Diagnosis:* Meckel's diverticulum with gastric mucosa and chronic penetrating ulcer."

COMMENT

Meckel's diverticulum was presumably described for the first time in 1683 by Raysch. Johann Friedrich Meckel explained this peculiar appendage of the ileum as an incompletely regressed ductus omphalomesentericus in 1808. His explanation is still accepted. In embryonic life this structure forms the connection between the alimentary canal and the yolk sac. Its persistence may give rise to various malformations. There may be incomplete involution of any part of this tubular structure resulting in umbilical sinuses, cysts, or a diverticulum attached to the ileum. The latter malformation is by far the most frequent and important, and the one with which we are particularly concerned.

The size of this diverticulum varies from 3 to 30 cm. in length. The width varies from 1.2 to 5 cm. at the base. The free end may lie loose in the abdomen; or it may be attached to the umbilicus or some other viscus. The walls are composed of all the intestinal coats. The mucosa usually resembles that of the ileum. However, numerous cases have shown islands of gastric or jejunal mucosa. Aberrant pancreatic cells have also been reported. Gastric mucosa is reported in from 12 to 52 per cent of the specimens examined by various authorities. These foreign cells are probably the result of faulty evolution from the primitive entodermal mucosa of the alimentary canal.

The diverticulum is usually found within one meter of the ileo-cecal valve in adults and .3 to .5 meters in the newborn, although its exact site is not constant.

The frequency of this congenital abnormality, as reported by a number of authors varies widely. Of 8,133 autopsies at the Dresden City Hospital, the incidence was 1 to 1000. At the Johns Hopkins Hospital 2,600 post mortem examinations showed an incidence of 1 to 173. Balfour reported fifteen cases in 10,000 subjects. Hall (1) reports ten in 357 laparotomies where the small intestines were examined. Montgomery (2) believes a conservative estimate is from 2 per cent to 3 per cent. The occurrence is predominantly in males in at least a 2 to 1 ratio. Christie found an association of other congenital malformations in over 30 per cent of cases of Meckel's diverticulum.

Hudson (3, 4) lists the following pathological changes described to date:

1. Gastric mucosa with ulceration
 - (a) without perforation, with hemorrhage
 - (b) with perforation, with or without hemorrhage.
2. Advancing point—presumable cause of intussusception.
3. Diverticulitis with acute inflammation and necrosis.
4. Intestinal obstruction other than intussusception.
5. Umbilical fistula.

The following rarely occur:

6. Tumor site.
7. Enterocystoma.
8. Duplex ileum.
9. Mesenteric cyst.
10. Tuberculosis of the ileum.

Although an uncomplicated Meckel's diverticulum is a harmless structure, from 30 to 70 per cent of the diverticuli give rise to symptoms. These may be divided into three principal clinical groups:

1. Profuse bleeding from a peptic ulcer in the diverticulum.
2. Infection of the diverticulum, both acute and chronic.
3. Intestinal obstruction.

The Peptic Ulcer Group. The aberrant gastric secreting cells are active and give rise to a peptic ulcer very similar in structure to the usual gastric or duodenal ulcers. Intestinal hemorrhage is the cardinal symptom of this group. The blood may be passed fresh, in clots, or may even be tarry. The bleeding may be persistent for long or short intervals. Abdominal pain may be present but it is usually vague. In infants there is usually no periodic colic, as is found in intussusception. An abdominal mass is usually not found on palpation. Perforation of the ulcer may occur and then the signs are those of diffuse peritonitis and sudden collapse. Perforation occurred in 56 per cent of thirty-four cases of this type collected by Greenwald and Steiner (5).

Infection. The symptoms resemble acute appendicitis so closely that differentiation is often impossible. The mechanism of infection and pathologic changes are very similar to acute appendicitis. A history of

bleeding is usually absent. The signs are those of an acute surgical abdomen, the point of maximum tenderness being either on the right or left side of the abdomen, and sometimes higher than in appendicitis. Hall (1) stresses the fact that the picture is more alarming and more rapidly advancing than in the usual case of appendicitis.

Intestinal obstruction. This may occur because of the presence of bands, kinking of the ileum at the base of an ulcer, or concomitant intussusception, the diverticulum being the base. The symptoms are those of intestinal obstruction. A history of melena may suggest Meckel's diverticulum as the cause.

Diagnosis. The diagnosis of the presence of a Meckel's diverticulum is rarely made preoperatively. It has been demonstrated radiographically only in older individuals on a few occasions. The cardinal symptom in the peptic ulcer cases is painless melena. The other conditions producing blood in the stool have to be considered in differential diagnosis. Gastric and duodenal ulcers usually occur in older children and X-ray evidence of the ulcer is found. Rectal polyps, adenomas and ulcerative colitis can be ruled out by proctoscopic examination. Intestinal bleeding in Henoch's or thrombocytopenic purpura or hemophilia is usually associated with bleeding into the skin. In intussusception there is marked colic and a tumor mass can usually be felt.

When bizarre abdominal pictures associated with infection are seen, Meckel's diverticulitis should be suspected and the ileum carefully explored, especially if the appendix does not show sufficient change to explain the picture. A preoperative diagnosis of diverticulitis is difficult and of academic interest only.

Prognosis. In uncomplicated and peptic ulcer cases without perforation, the prognosis is good if early surgery is applied. A mortality of 7.6 per cent is reported by Greenwald and Steiner (5). In cases where perforation is present the prognosis is very serious. A 46 per cent mortality is reported by the same authors. In cases complicated by intestinal obstruction the mortality is 25 per cent. The prognosis in the individual case depends a good deal on early diagnosis, followed by immediate surgery.

Treatment. All diseases of Meckel's diverticulum need immediate surgery. Diverticulectomy is preferred to excision of the intestinal segment. The danger of perforation, associated with peptic ulcer, is great, and this makes early exploration advisable in any case where the diagnosis is suspected. Careful postoperative care, including infusions of glucose solution and blood transfusions, is essential.

CASES ADMITTED TO THE MOUNT SINAI HOSPITAL 1926-1937

Among the 150,000 patients admitted to this hospital during the eleven year period from 1926 to 1937, the ten cases shown in table 1 were found to be admitted with symptoms due to a Meckel's diverticulum.

TABLE I

YEAR	AGE	SEX	SYMPTOMS	PAST HISTORY	OPERATION	PATHOLOGY	RESULT
Children							
1926*	26 mos.	Male	Abdominal colic; vomiting; repeated bright and dark blood	Four previous admissions for same complaints	Diverticulectomy	Peptic ulcer	Well
1928*	15 mos.	Female	Pallor; vomiting; melena	None	Ileostomy; diverticulectomy	Peptic ulcer	Well
1932	10 years	Male	Pain L.L.Q.; vomiting; diarrhea	None	Diverticulectomy	Gangrenous diverticulum. No ulcer	Well
1934	2½ years	Male	Melena	Several previous attacks of melena	Diverticulectomy	No ulcer. (Attached to umbilicus)	Well
1934**	7 years	Male	Periumbilical vomiting	Similar attack 7 wks. before	Diverticulectomy; reduction of ileal intussusception	No ulcer. Gastric mucosa present	Well
1935	16 years	Male	Melena; x-ray positive	Previous melena	Diverticulectomy	No ulcer. Gastric mucosa	Well
1937***	10 mos.	Female	Melena; x-ray negative	Previous melena	Diverticulectomy	Peptic ulcer (chronic); gastric mucosa	Well
1937	11 mos.	Male	Melena	Previous melena	Diverticulectomy	Peptic ulcer (chronic); gastric mucosa	Well
Adults							
1932	37 years	Female	Periumbilical pain; intestinal obstruction	None	Diverticulectomy relieving partial intestinal obstruction	No ulcer	Well
1934	45 years	Female	R.L.Q. pain	Typical gall bladder history	Diverticulectomy, cholecystectomy	No ulcer	Well

* Reported by Aschner and Karelitz (8).

** Reported by Klingenstein (10).

*** Case reported in detail herewith.

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SYPHILIS TRANSMITTED BY TRANSFUSION

SAMUEL H. AVERBUCK, M.D.

Transfusion of blood in the treatment of many conditions, and in the varied stages of disease, has become a very commonly employed therapeutic aid. Obviously, the transferred blood should be free of organisms or their products or any abnormal concentration of the usual blood constituents. For this reason, there have been evolved systems of donor control which, although varying in slight detail, have for a common goal, the estimation and periodic rechecking of the health of classified blood donors.

It has long been recognized that one of the gravest accidents to be prevented in transfusing blood is the transmission of syphilis. For this reason, it has been customary for donor agencies to do serologic retesting and reexamination of donors at varied intervals. In spite of the awareness of this danger of disease transmission, and the safeguards conceived to prevent the special hazard of syphilis inoculation, there have been published recently many instances of syphilis transmitted by transfusion. All who are interested in this problem agree that the actual incidence of this tragic sequela far exceeds the reported occurrence.

The following case is being added to the published reports because it occurred under well-controlled conditions, and emphasized the need for further protective measures which have since been instituted.

CASE REPORT

History (Adm. 406129). S. B., a sixty-one year old housewife, had had herpes zoster involving the left lower extremity, five months before coming under observation. After the subsidence of this condition, she began to experience increasingly severe lower back pain. There were no significant associated symptoms. The past history included the record of an appendectomy which had been done thirty years before, and the incision and drainage of a breast abscess and metastatic abscess in the right hip region many years ago. The patient had been married forty years, and had given birth to four children. There had never been a miscarriage. Menopause had occurred sixteen years before. Her husband died in this hospital six years previously of a carcinoma of the colon with bone metastases. His blood Wassermann was negative.

Examination. The patient was a chronically ill, pale, elderly, woman. The pupils were equal and regular, and reacted promptly to light and accommodation. The heart and lungs were normal. None of the ab-

dominal organs were palpable, and there was no adenopathy. The neurological examination was negative. There was marked tenderness over the fourth lumbar vertebra. No other bony tenderness was demonstrable.

Laboratory data. The hemoglobin was 65 per cent (Sahli), with 4,400,000 red blood cells, and 7,500 white cells. The differential blood count showed 68 per cent polymorphonuclear neutrophils, 28 per cent lymphocytes, and 4 per cent monocytes. The systolic blood pressure was 100; the diastolic, 70. The stool and urine examinations were negative. Bence-Jones' protein was not present in the urine.

X-ray examination of the spine by Dr. Leopold Jaches, was reported, in part, as follows: "The most definite pathologic change, however, is the marked bone absorption of the fourth lumbar vertebra, affecting particularly the anterior two-thirds. This finding is definite evidence of malignancy, probably metastatic."

Course. Although a primary growth was not located, radiotherapy to the spine was given for the relief of pain. This proved surprisingly effective, considering the diagnosis, and in a few weeks the patient was able to move about comfortably. The spleen now became palpable for the first time, and in the next few months enlarged rapidly. The anemia and cachexia progressed. The spleen size was reduced considerably by radiotherapy. Now, some anterior cervical nodes became palpable on the left side of the neck. One of these nodes was excised by Dr. P. Klingenstein, and was described as "hyperplastic lymphadenitis" by Dr. P. Klemperer.

Because of the effectiveness of radiotherapy, the splenomegaly and adenopathy, the secondary anemia, and the inability to find a primary neoplasm, the diagnosis considered most probable was Hodgkin's disease. Periodically, when the anemia became marked, citrate transfusions of 500 c.c. of blood were given.

On June 24, 1937, a 500 c.c. citrate transfusion was given by the gravity method. The donor, who, on cursory examination, appeared well, was obtained from one of the largest accredited donor agencies in the city. Both donor and recipient were in Group II A (Jansky), and were compatible in the cross agglutination test.

There was no immediate post-transfusion reaction. Five weeks after this transfusion, the patient noticed the appearance of large, red, indurated, tender, somewhat raised lesions on the fingers, shoulders, abdomen, and back. Some of these soon became open sores which persisted as shallow, moist, indolent ulcerations. Intractable and severe headache which was worse at night, sore throat, a slight cough, generalized body and bone aches and pains, and temperature elevations characterized the clinical picture. A few days later, a diffuse, maculopapular rash appeared, and lymph nodes became palpable in the inguinal, axillary and posterior

cervical regions. The diagnosis of syphilis in the secondary stage suggested itself, and was confirmed by positive serological evidence—blood Wassermann and Kahn tests both being reported 4 plus. Dr. Isadore Rosen's description at this time follows—"Patient presents a typical universal maculopapular eruption characteristic of secondary lues. The clinical features are so definite that one identifies this eruption without any other evidences, such as a primary lesion, which is not present in this case. The patient presents, also, a universal glandular involvement which is usually associated with this disease in this stage. The palmar and plantar lesions are also one of the characteristic corroborative features. Also, patient complains of marked aggravation of headache at night which is seen in this early stage."

Bismuth therapy was instituted, and after four injections (totaling 3.5 c.c.) of bismuth subsalicylate were given intramuscularly, the rash faded, the larger shallow ulcerations healed, the headache, cough, and generalized aches and pains disappeared, and the temperature subsided. Further bismuth and arsenic therapy was continued.

Careful consideration suggested only one possibility, i.e., that the syphilitic infection was introduced by direct inoculation by transfusion. The donor was recalled, and his blood obtained for serological examination. Wassermann reaction was 4 plus, Kahn, 3 plus. More complete examination revealed no semblance of a rash, nor of a genital lesion or scar. The donor denied any history of a recent illness. Investigation disclosed that on May 11, 1937, six weeks before, he had given blood for a transfusion which was uneventful. On June 11, 1937, two weeks before he served the patient discussed here, his blood Wassermann reaction was negative. Furthermore, five weeks later on July 29, 1937, a blood test performed directly before a transfusion at a New York hospital, showed a two plus reaction. In spite of this rejection, the donor gave blood the following day, July 30, 1937, to a patient in another hospital where serologic testing was not done. This patient died a few days later. Finally, following notification to the donor bureau of the events which had occurred to the author's patient, the donor was recalled, and his blood donor's book taken from him. After confirmatory serologic tests, anti-luetic treatment was begun and is continuing currently.

The subsequent course of the patient's illness seemed to be accelerated. The anemia and cachexia became more marked. Bone involvement, then a pathological fracture of the left humerus developed, and finally, a few months later, the patient died.

Necropsy findings. It is not relevant here to describe the details of the systemic disease, which was considered to be an unusual form of Hodgkin's disease. However, nowhere was there evidence of any syphilitic lesions. It was definitely established that tertiary lues could not have been present.

DISCUSSION

It is important when presenting a case of transfusion syphilis to establish the fact that the patient did not have lues before transfusion. Although no serologic test had been done, it is clinically quite clear that an elderly woman with the history as recorded was not luetic. Furthermore, the illness she contracted five weeks after receiving blood from a donor, later proved to be syphilitic, was the secondary stage of syphilis. The manifestations appeared five weeks after inoculation with infected blood. This incubation duration comes within the limit described by other observers, i.e., four to fourteen weeks, and characteristically, there was no primary lesion. Post mortem examination revealed no evidence of advanced or tertiary lues. It is an inescapable conclusion that the syphilis demonstrated in its second stages by the patient was introduced into her blood stream through the medium of the donor's infected blood. No other source of infection was possible.

Many such authenticated cases have been published. Rein (1) mentions that medical literature contains records of sixty-eight cases, with many more known, but unpublished. It is especially significant that the instance here presented occurred in spite of a background of controls and regulation which has been considered completely adequate. This emphasized the need for an even more efficient system. The events related above point out the most effective method of syphilis prevention. The only time that this infected individual was restrained from acting as donor was in an institution that performed an immediate pre-transfusion serologic test. In all other instances, it was assumed that he was free of infection because he came from an accredited donor agency.

The unfortunate victim of this tragic accident was already afflicted with an incurable and fatal disease. Although adding greatly to her misery and unhappiness, it is questionable whether this additional condition actually hastened the ultimate issue. Transfusions are done so frequently in stages of so many curable conditions that the special and consoling circumstances in this case must be considered exceptional. They rather emphasize the more usual, optimistic situations which would heighten the tragedy of transfusion syphilis.

DONOR CONTROL

Until recently the New York City Board of Health regulations controlling donor agencies required a serologic test every six months. In 1937, this interval was reduced to three months. A few of the hospitals which still control their own donors, and some of the smaller professional agencies, retest every six weeks. Yet, even with this shortest interval it is possible for an individual to contract transmissible syphilis without manifesting a visible primary lesion or other signs of lues. As Morgan (2) has pointed out, transfusion syphilis is transmitted by blood from donors who

are in the incubation period or in the primary or secondary stages of the disease. The usual interval from exposure to the appearance of the chancre is about four weeks. It must be recalled that the primary lesion may not be visible or may not occur at all. The most common serologic test employed—the Wassermann reaction—becomes positive from two to four weeks after inoculation. Obviously, there is a short period when an individual may have, unknown to himself, and undetectable by the usual methods, a syphilitic infection which conceivably could be transmitted by direct inoculation. Therefore, it would appear desirable to test all donors with the most sensitive test available, consistent with such factors as time, ease and practicability of execution, and to apply this most sensitive test as recently before the anticipated transfusion as possible. Flocculation tests, such as those described by Kahn and by Kline, have been proved to possess the required specificity and the desirable sensitivity. They possess the added advantage that they can be done in a very short time with very little blood. One of the objections often ascribed to the flocculation tests, particularly the Kline, is that they give false positive results. Undoubtedly, a drawback in other circumstances, this "over-sensitivity" would appear to be a distinct aid in excluding questionable donors. The Kline test is particularly suitable, for with its high sensitivity, a negative reaction would surely exclude syphilis. The more accurate and trustworthy complement fixation tests could then be performed later to determine definitely whether or not the subject had syphilis. In the meantime, the possible transmission of the infection would have been avoided.

Transfusions are rarely of such urgent necessity that the time required for the performance of a flocculation test for syphilis could not be granted. Where traumatic shock or hemorrhage makes replacement of circulating fluid volume immediately essential, intravenously administered physiologic or hypertonic saline or glucose solution can serve as a satisfactory temporary expedient.

Rein, who has been an ardent protagonist for the immediate pre-transfusion testing of grouped donors, suggests the following procedures, all of which can be done in thirty minutes.

- A. Establish the blood group of all volunteer donors and regroup all professional donors.
- B. Determine the suitability of the donor's blood for the recipient by cross matching.
- C. Detect the presence of syphilis serologically by means of the very sensitive and specific Kline (or Kahn) diagnostic and exclusion flocculation tests.
- D. Detect any clinical evidence of syphilis by means of an adequate physical examination.

Although there is some evidence that the use of blood from donors with late or tertiary stages of syphilis is without danger of transmission of the

disease, there is usually so plentiful a supply of potential donors that this practice need never be necessary.

Arising from the investigation following this instance of syphilis transmitted by transfusion, it was learned that, "in at least fifty-seven hospitals, neither a physical examination nor a serological test is done" on prospective blood donors, and that "only fourteen hospitals reported doing both," whereupon, the largest donor agency in this city called to the attention of hospitals and physicians using its service the necessity for doing a rapid serological test for lues immediately prior to transfusion. Final responsibility rests not with the donor-supplying agency, but with the physician performing the transfusion.

In this hospital, the following new rule governs this aspect of transfusion:

"Any transfusion given in the Hospital must be preceded by the Kline or Kahn test, as well as by a physical examination of the donor. Exception is to be made only in emergency cases where even the few minutes extra time required for these procedures would jeopardize the life of the patient."

There is every reason to expect that these newly instituted regulations will prevent the further transmission of syphilis by transfusion in this hospital.

SUMMARY

A case of transmission of syphilis by transfusion is described. All the characteristics of transfusion lues, i.e., the usual incubation period, the absence of a primary lesion, the appearance of the secondary stage of the disease, were present. The donor was proved luetic, and the patient infected was proved not to have had lues previously.

Defects in the system of donor serologic control are discussed, and it is emphasized that the surest safeguard against a repetition of such an accident is immediate pre-transfusion serologic testing of all donors by a rapid, sensitive flocculation test, such as the Kline or Kahn.

As a result of this instance of transfusion syphilis, such recommendations have been made to the hospitals of New York City, and are in force in this institution.

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ABSENCE OF OCCULT BLOOD IN THE STOOLS IN THREE CASES OF GASTRIC CARCINOMA

MARCY L. SUSSMAN, M.D.

[From the Department of Radiology, Service of Dr. Leopold Jaches]

Crohn (1) states that "the presence of occult blood in the feces is an important diagnostic sign in the diagnosis of gastric carcinoma since its absence on repeated testings definitely diminishes the likelihood of the presence of a gastro-intestinal new growth." This author states that occult blood is present in about 90 per cent of the cases of gastric carcinoma. Hence, the occurrence of three cases with repeatedly negative guaiac tests on the stool within a relatively short period of time are worthy of note.

CASE REPORTS

Case 1. T. B., (Adm. 412757) a Russian housewife, 65 years of age, was admitted on August 13, 1937 and on September 15, 1937, with the *final diagnosis* of carcinoma of stomach; severe secondary anemia; confluent bronchopneumonia in the right lower lobe and left lower lobe.

History. The *past history* was essentially negative. There was dyspnea on exertion which appeared after climbing two flights of stairs. There was occasional palpitation and slight edema of the legs in the evening, which disappeared on resting. *Three weeks* before admission the patient complained of generalized weakness, drawing pains in the feet, numbness and tingling of the hands. There was progressive pallor. *One week* before admission a small amount of blood was seen in the stool; this did not recur. Five days later she vomited once.

Examination. The patient was an obese woman with a pale, yellow, puffy skin. The tongue was markedly atrophic. The chest was clear. The heart was slightly enlarged to the left mid-clavicular line. There was a systolic murmur at the apex. The heart sounds were normal. The liver was palpable three finger-breadths below the costal margin. The spleen was not enlarged. Pelvic examination was negative. Rectal examination revealed a black stool. The abdominal reflexes were absent; the deep reflexes were present. There was a bilateral Babinski but no Hoffman sign, and the vibration sense was absent from the iliac crests down. Pin-prick perception was present throughout.

Laboratory Data. Blood pressure was 124 systolic and 64 diastolic.

Hematology: hemoglobin 30 per cent; red blood cells, 2,300,000; platelets, 350,000; white blood cells, 5,850; polymorphonuclear leucocytes, 79 per

cent; reticulocytes, 7 per cent; cell volume, 12 per cent, an estimation which was interpreted as indicating severe hypochromic anemia.

Blood Chemistry: Urea nitrogen, 13 mg. per 100 c.c.; sugar, 90 mg. per 100 c.c.; cholesterol, 210 mg. per 100 c.c.; icteric index, 2; bilirubin, 0.2 mg.

The Van den Bergh test was negative. *Exton test:* (1) 90; (2) 140; (3) 160.

Urine analysis: The urine showed a slight trace of albumin, urobilin 1:2; there was no bile. There was a large number of white blood cells, occasionally clumped; also a few red blood cells; the specific gravity was 1010.

Rehfuss test meal: There was no free hydrochloric acid even after injection of histamine. On the fasting specimen the guaiac test was 4 plus. The next five specimens were negative. The last five specimens were 4 plus.

Electrocardiogram showed sinus tachycardia with left ventricular preponderance; large Q₁; QRS low; RT depressed in lead II; T₃ semi-inverted. The changes indicated an abnormality in the ventricular musculature.

Sternal aspiration revealed a fatty marrow with hyperplasia of the normoblastic element, such as is seen in severe secondary anemia.

Course. Two transfusions were given raising the hemoglobin to 58 per cent. Eight stools were negative to the guaiac test. The gastro-intestinal examination was incomplete because the patient could not be fluoroscoped, but on the films alone no abnormality was demonstrated.

Roentgen examination of the chest revealed an enlarged heart and evidence of pulmonary congestion.

The patient died three weeks later with bilateral bronchopneumonia.

Necropsy Findings (P. M. 10521). Carcinoma of the stomach with metastases to omentum, liver, lung, and regional lymph nodes was found. The carcinoma was polypoid with a few, small, shallow ulcerations. Rheumatic heart disease, interstitial valvulitis of mitral and tricuspid valves were also present.

Case 2. B. L. (Adm. 414308) a Porto-Rican housewife, 38 years of age, was admitted on September 20, 1937 and died on October 5, 1937, with a *final diagnosis* of carcinoma of the stomach with generalized metastases and lymphangitic carcinoma of the lungs.

History. One year before admission the patient developed a continuous, dull, aching pain in the epigastrium radiating to the back, with a sense of bloating and frequent eructations. There was an occasional mild, non-productive cough.

She had had a cholecystectomy and an appendectomy performed five months before admission because of abdominal complaints, without relief of symptoms. Thereafter she noted an increase in her cough; there was progressive dyspnea and tachypnea and she lost twelve pounds in weight.

Examination. The patient was a thin, sallow, middle-aged, white

female, dyspneic and orthopneic, with a paroxysmal cough. There were dullness over both apices, showers of moist crepitant râles over both lungs, especially on the left, and bronchovesicular breathing at the left apex anteriorly. The heart was normal. The liver was palpable one finger-breadth below the costal margin. There were no abdominal masses and no ascites. Rectal examination revealed a hard, nodular mass high on the anterior wall.

Laboratory Data. Blood pressure was 120 systolic and 86 diastolic.

Hematology: hemoglobin, 83 per cent; white blood cells, 13,500; polymorphonuclear leucocytes, 71 per cent.

Blood chemistry: Urea, 10 mg. per 100 c.c.; sugar, 110 mg. per 100 c.c. The blood Wassermann test was negative.

Sputum examination was negative for tubercle bacilli.

The stool was repeatedly guaiac negative for occult blood. Urine analysis showed no abnormality. The gastro-intestinal examination by a barium meal revealed a deformity of the gastric air bubble due to a neoplastic mass.

Roentgen examination of the chest revealed a diffuse infiltration, presumably due to a lymphangitic carcinosis.

Necropsy Findings (P. M. 10553). Examination revealed a scirrhus carcinoma of the cardiac end of the stomach with extension to the esophagus and pancreas, with metastases to the regional lymph nodes, right adrenal, both ovaries, kidneys, ureterosacral ligament, cul-de-sac, and peritoneum. The carcinoma showed a few small shallow ulcerations on the lesser curvature. There was a lymphangitic carcinosis of the lungs and pleura; hypertrophy of the right ventricle and auricle; chronic passive congestion of the liver and kidneys.

Case 3. I. H., (Adm. 414722) an Austrian male, 63 years of age, was admitted on September 29, 1937 and discharged on October 7, 1937, with a *final diagnosis* of carcinoma of the stomach.

History. The patient complained for three years of repeated episodes of nausea and vomiting with occasional epigastric distention. He had no temperature, abdominal pain, or melena. Four days previous to admission he experienced a similar episode with hematemesis.

Examination. The patient was a small, somewhat emaciated man, in no distress. There were several discreet small glands in the right axilla. The lungs were clear. The heart was not enlarged; the sounds were good. There was a systolic murmur at the apex; the rhythm was regular. The liver was just palpable. The abdomen was negative. Neurological examination was negative.

Laboratory Data. *Hematology:* hemoglobin, 83 per cent; white blood cells, 7,000; polymorphonuclear leucocytes, 72 per cent.

Blood Chemistry: Urea nitrogen, 16 mg. per 100 c.c.; sugar, 90 mg. per 100 c.c. The blood Wassermann test was negative.

Urine analysis: No abnormality was found.

Rehfuess test meal revealed an achlorhydria. No histamine test was done.

Guaiaec test on the stools revealed no evidence of occult blood. The examination was not repeated.

An *electrocardiogram* showed evidence of slight myocardial damage.

The *barium meal* examination revealed a mass in the cardia due to a neoplasm.

Course. The patient signed out against advice. No exploration was done.

COMMENT

Two of the three cases gave a history of either melena or hematemesis and, in spite of this, repeated examinations failed to reveal occult blood in the stools. It is difficult to attribute this to repeated technical error and yet another explanation does not suggest itself. In any event, these cases illustrate that repeatedly negative guaiac tests do not, by any means, rule out the diagnosis of gastric carcinoma, even though it is stated that "almost always occult blood is persistently present in the feces"(2). It is likely that non-ulcerating neoplasms are less apt to show occult blood in the stools. It is interesting, too, that in one case the carcinoma was not visualized radiographically; however, a satisfactory examination could not be made in this case.

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Joseph F. Cullman

December 23, 1854–August 1, 1938

The death of Joseph F. Cullman on August 1, 1938, brought to a close one of the longest periods of active service of a Trustee to The Mount Sinai Hospital. Coming in 1897 to the old Mount Sinai Hospital, then located at 67th Street and Lexington Avenue, Mr. Cullman found a small, but already famous hospital. Though small in comparison with the hospitals of to-day, it was large in comparison with other privately supported hospitals of that period. Already in its forty-fifth year of existence, the Hospital had long since achieved an international reputation for its charity and the quality of its scientific service. The hospital staff, as Mr. Cullman first knew it as a Trustee, consisted of eighty-eight physicians for the in- and out-patients. Eleven young physicians comprised the house staff.

Trustee service, however, cannot be measured merely in terms of years; it must be evaluated in the quality and character of the service. By this test, Mr. Cullman's service to the Mount Sinai Hospital was of the greatest value. He served on many important committees, in which his participation turned quickly from one of observation and study to that of active work. He contributed generously of his means to the several building funds during his forty-one years of service.

His major hospital interest was in the field of medical education and perhaps his most significant contribution as a Trustee was his service as Chairman of the Board's Committee on Medical Education. In order to place this important phase of the Hospital's work on a sound basis, he urged the creation of an endowment fund for this purpose and made the first substantial contribution of \$25,000 toward its support in 1922. This initial gift gave marked impetus to the then inchoate hospital program of medical education and led, in the following year, to the present arrangement with Columbia University for placing the Hospital's post-graduate medical instruction on a university basis.

The first requisite of a trustee is devotion to the interests of the institution which he serves. This trait Mr. Cullman had in full measure. His death on August 1st was keenly felt but there is consolation in the knowledge that the work which he initiated will continue as long as Mount Sinai exists.

Joseph Turner

CLINICAL PATHOLOGICAL CONFERENCES

GEORGE BAEHR, M.D. AND PAUL KLEMPERER, M.D., *presiding*

Wednesday, December 15, 1937

Case 1. Pulmonary Tuberculosis in a Man of Seventy-Seven. Congestive Heart Failure Due to Chronic Pulmonary Tuberculosis and Emphysema. Patent Urachus with Urachus Fistula. Carcinoma of the Prostate Arising after Resection of a Prostatic Adenoma

(From the Medical Service of Dr. B. S. Oppenheimer)

History. (Adm. 410226; P.M. 10417) The patient, a seventy-seven year old man, entered the hospital with a history of gastric complaints since early youth. These included post-prandial pain which was relieved by bicarbonate of soda. Nine years before admission, he suddenly developed severe abdominal pain and was operated upon for a perforated duodenal ulcer. The ulcer was sutured and the patient remained well, except for occasional attacks of gross hematuria, until about three weeks before admission. He then began to have exertional dyspnea and five days before entrance noted increasing ankle edema.

Examination. The patient was a well-developed, acutely ill male with marked dyspnea, orthopnea, peripheral cyanosis, and edema of the eyelids and legs. The chest cage was emphysematous in type and numerous fine râles could be heard throughout the lungs. Heart sounds were distant. Blood pressure was 160 systolic and 90 diastolic. The liver edge was felt 4 finger-breadths below the costal margin. The prostate was tremendously enlarged and firm. In the lower abdomen, just to the right of the midline, a hard, tender, rectangular mass was found, extending from the pubis to within 3 cm. of the umbilicus. Catheterization failed to alter its size.

Laboratory Findings. Hemoglobin, 35 per cent; red blood cells, 2,300,000; white blood cells, 23,000 per cu. mm., (90 per cent polymorphonuclear leucocytes). Venous pressure was 16 cm. of water. Urine contained a trace of albumin and great numbers of red blood cells. An electrocardiogram showed evidence of left ventricular preponderance and abnormality of the ventricular muscle. Blood urea nitrogen was 65 mg. per 100 c.c. Blood Wassermann reaction was negative.

Course. The clinical impression was carcinoma of the urinary bladder with metastases to the abdominal wall, hypertrophy of the prostate, and atherosclerotic heart disease with congestive heart failure. Immediately after admission, a phlebotomy of 300 c.c. was performed; 50 c.c. of 50 per cent glucose was administered intravenously with improvement of the cardiac status. Further examination revealed dulness with prolonged breath and voice sounds over the right upper lobe. An X-ray examination showed a dense shadow over the uppermost portion of this lobe with marked pleural thickening, interpreted as indicative of an old fibroid tuberculosis. The sputum was found to contain numerous tubercle bacilli. As the patient's condition showed some improvement, an attempt was made to

determine the nature of the abdominal mass. The urological consultant suggested that it might represent obliterated hypogastric vessels. Shortly thereafter, the mass diminished considerably in size so that only a cord-like structure could be felt. The patient began to fail, however, became stuporous, lethargic, eventually comatose, and died ten days after admission.

Necropsy Findings. The heart weighed 400 grams. The right ventricular chamber was markedly dilated and its wall moderately thickened. The other chambers showed slight to moderate dilatation. There was only moderate coronary arteriosclerosis but no narrowing. The *pleura* over the anterior surface of the right upper lobe and the apex of the left upper lobe was thickened. Directly beneath the pleura of the apical segment of the upper lobe of the *right lung* was an irregular, firm area about 2 by 2 by 1.5 cm. On section this showed a mottled black and gray surface in which were found several small cavities from 2 to 5 mm. in diameter. Microscopic study disclosed active tubercle formation with caseation, but only a few bacilli. All the *pulmonary* lobes contained firm, airless, grayish-white, granular, indistinctly circumscribed, peribronchial areas. These were usually the size of cherry pits. Some of them were only from 3 to 4 mm. in diameter. The nodules were numerous in all except the left lower lobe. Microscopic examination proved these to be foci of tuberculous bronchopneumonia loaded with tubercle bacilli. The axillary portion of the right upper lobe contained a calcified anthracotic nodule one centimeter beneath the pleura. One tracheobronchial node showed calcification and active tuberculosis. There was cylindrical bronchiectasis of both upper lobe bronchi. The right *kidney* weighed 100 grams, the left 170 grams. The surfaces of both were finely granular. The pelves and calyces were markedly dilated; their mucosae were thickened and injected. The *ureters* similarly were dilated and their mucosae thickened. Situated in the midline of the lower abdomen between the rectus muscles and the parietal peritoneum, was a firm cylindrical cord-like structure, 2 cm. in diameter. It extended from a stout attachment on the symphysis pubis and the vertex of the bladder to the umbilicus where it faded into the anterior abdominal wall. Cut section revealed a central fistulous tract. Microscopic study confirmed the gross impression of urachal fistula. From the area of attachment of this mass to the bladder, a septum projected posteriorly to the vertebral column dividing the lower abdominal cavity into left and right halves. The loops of small intestine lay entirely within the left half. The *bladder* wall was markedly thickened (2 cm.). The mucosa was injected and trabeculation was prominent. Projecting into the bladder was a large firm nodule of *prostatic tissue*, 4 cm. in diameter. Sectioned surface of this and of the markedly enlarged lateral lobes presented the picture of fibroadenomatous hyperplasia. The adenomatous portions could be readily distinguished from the compressed remnant of prostatic tissue proper at the periphery of the gland. Histologic preparations, however, of this compressed portion revealed a small carcinoma. The veins of the prostatic plexus were thrombosed. On the posterior wall of the duodenum just beyond the pyloric rim was a healed ulcer with smooth slightly elevated edges. It extended to the serosa which was thickened at that site.

Comment. Dr. Klemperer: The tuberculosis in the right lung was definitely progressive while that in the left lung was more dormant. The point should be emphasized that even here the evidences of activity were apparent. Chronic fibroid tuberculosis with areas of active disease is found typically in older indi-

viduals. The marked right ventricular hypertrophy was most likely the result of the severe emphysematous changes in the right lung. Attention should be drawn to the fact that the prostatic carcinoma, as in most cases, had been found not in the area of the fibroadenomatous hyperplasia but in the thin remaining shell of prostatic tissue enclosing the hypertrophied portion. This has practical significance in that a surgeon shelling out a fibroadenoma may leave a carcinoma behind in the capsule. The chief factors leading to the fatal outcome in this case, were the emphysema and tuberculosis.

Dr. Baehr: The increased incidence of tuberculosis at this hospital in the last few years is of significance, as is also the fact that for the first time in many years, tuberculosis increased in New York City in 1936 while in the rest of the state it had continued to fall. This state of affairs is in part due to the inadequacy of hospital facilities for individuals with tuberculosis in New York City, as contrasted with the adequate facilities of hospitalization available to patients elsewhere in the State. Most tuberculosis patients admitted to hospitals in this city are already in a moderately advanced or late state. This, he felt, was another factor in the increased incidence.

Some surgeons have opposed the transurethral resection of prostatic adenoma because it may leave behind an unsuspected carcinoma. This case illustrates that even the shelling out of a large adenoma by the suprapubic route may leave behind enough prostate tissue in the bed of the prostate to give rise later to carcinoma.

Case 2. Lymphosarcomatosis of Intestine. Multiple Intussusceptions

(From the Medical Service of Dr. B. S. Oppenheimer)

History. (Adm. 411837; P.M. 10453) The patient, a 43 year old chauffeur, had been in good health until four months before admission. At that time, he developed an upper respiratory infection followed by paroxysmal cough, productive of a small amount of sputum, increasing fatigue, and exertional dyspnea. Nine weeks before entrance, he noted a cherry-sized mass on the upper portion of his back. Incision of this mass yielded no pus, and it continued to grow. A week later, another swelling appeared in the left axilla. Three days before admission, the patient developed severe right abdominal cramps. The pain gradually shifted to the left and was followed by profuse, bloody diarrhea which continued at the rate of about seven movements per day until he came to the hospital. During this period, his abdomen increased in size and edema of the feet was noted. The patient stated that he had lost twenty-five pounds since the onset of his illness.

Examination. The patient was a cachectic and markedly anemic male. In the left axilla an egg-sized, firm, freely movable, non-tender mass could be felt. The veins over the upper chest were slightly dilated. Over the left upper lobe, both anteriorly and posteriorly, resonance was impaired and breath sounds were bronchovesicular in character. Râles were not heard. The abdomen appeared moderately distended. The liver could be percussed two finger-breadths below the costal margin. The spleen was not palpable. At the level of the ninth dorsal vertebra just to the left of the midline, was a soft, non-tender, reddish-blue, papillary tumor with an ulcerated surface. There was slight clubbing of the fingers. Pitting edema was noted over the right arm and over the ankles extending as high as the level of the xiphoid.

Laboratory Data. Hemoglobin, 47 per cent; red blood cells, 3,000,000; white blood cells, 30,250 (78 per cent polymorphonuclear leucocytes, 13 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophiles, and 1 per cent myelocytes). The stool was fluid, brown, and contained occult blood. Venous pressure was 10 cm. of water in both arms. Blood Wassermann reaction and chest X-ray examinations were both negative.

Course. The patient was seen by a dermatologist who felt that the mass in the dorsal region might be mycosis fungoides or a neoplasm of the lymphoblastoma group. The mass was therefore excised and examination revealed it to be a *reticulum cell lymphosarcoma*. Five days after admission, the patient suddenly went into shock and developed marked abdominal distension. There was no vomiting. A friction rub became audible over the pericardium. The possibilities of the presence of an acute pulmonary embolus or bronchopneumonia with pleurisy were considered. Death occurred the same night.

Necropsy Findings. The mucosal folds of the *duodenum* were thickened throughout, due to an infiltration with grayish-white cellular tissue. In the descending portion there was a large, polypoid tumor 6 cm. in diameter, elevated above the surrounding mucosa about 2 cm., and a smaller one 3 cm. in diameter. Section of these revealed the same grayish-white cellular background. These tumors appeared to be extreme exaggerations of the variety of infiltrations found in the remainder of the duodenal rugae. In the upper *jejunum*, similar giant rugae and tumor formations were seen here and there with superficial ulceration. The lesions were noted with decreasing frequency beyond the first three feet of jejunum. There were three intussusceptions within the *ileum*, each associated with a zone of neoplastic infiltration. The final loop of terminal ileum contained a group of polypoid tumors similar to those found within the duodenum. The right lobe of the *liver* contained two grayish-white nodules approximately one centimeter in diameter. One of these was sharply demarcated; the other was more infiltrative. The posterior part of the left lateral wall of the *larynx* contained a sessile polypoid tumor 4 cm. in diameter which on section was seen to be composed of grayish-white cellular tissue. It infiltrated the *trachea* and produced an extension upward to the right side of the larynx. In the left lobe of the *thyroid* was a sharply defined grayish-white tumor nodule 0.5 cm. in diameter. Microscopic examination of these various tumors revealed them to be lymphosarcoma of the reticulum cell type. Tumor giant cells were numerous.

Comment. Dr. Klempner: This neoplasm is derived from a primitive cell type and hence could be expected to grow rapidly and metastasize widely. Involvement of the trachea and larynx is rare. At this hospital, tumor giant cells in lymphosarcomatosis have been an uncommon finding, but several cases in which they were found have been reported from Presbyterian Hospital.

Dr. Baehr: The polypoid type of tumor found in the intestine in this instance is rare in lymphosarcoma. The typical intestinal lesion is flat and infiltrative with destruction of the muscularis leading to aneurysmal, pouch-like dilatation of the involved wall. Hence intestinal obstruction is unlikely. In this case the intussusceptions which resulted in intestinal obstruction were produced by multiple polypoid intestinal tumors.

Reported by ARTHUR SELIGMANN, JR., M.D.

Wednesday, December 22, 1937

Case 3. Typhoid Fever

(From the Medical Service of Dr. George Baehr)

History. (Adm. 417108; P.M. 10605) The patient was a 37 year old, married male who had been well until three weeks before admission. At that time he developed severe crushing pain in the back of the neck and generalized aches and pains. His temperature was found to be 102.5°F. The pains soon disappeared, but the fever persisted with an evening rise to 103°F. and a usual fall to 99°F. in the morning. Profuse night sweats appeared. Two weeks before admission he noted the presence of red spots over the trunks and arms, which faded gradually. The patient stated he had not been out of the city for six years. There was no history of typhoid contact.

Examination. The patient was a well-nourished, well-developed, acutely ill, pallid male, perspiring profusely. The heart and lungs were normal. The edge of the spleen was palpable, just at the lower border of the costal margin. A few maculopapular, erythematous spots which faded on pressure were seen in the skin of the chest, abdomen, and arms.

Laboratory Data. Blood hemoglobin, 88 per cent; white blood cells, 8,300 per cu. mm. (polymorphonuclear leucocytes, 68 per cent; lymphocytes, 23 per cent; monocytes, 9 per cent). Sedimentation rate, 59 minutes. An electrocardiogram disclosed sinus tachycardia, left ventricular preponderance, a large Q3, low T2, and inverted T3. A chest X-ray examination was negative. Urine showed a trace of albumin and rare hyaline casts. Urobilinogen was present in 1 to 20 dilution. Blood Wassermann reaction was negative. Blood agglutinations revealed agglutination of 1 to 1280 for the Mount Sinai strain of bacillus typhosus. Repetition of this procedure several days later was again positive. Blood culture revealed the presence of *B. typhosus*.

Course. The temperature on admission was 103.6°F.; it gradually rose, reaching 105.6°F. on the sixth day of hospitalization and remained at about that level during the fourth week of his illness. Five days after admission his stool became grossly bloody and the guaiac reaction markedly positive. Prior to this time, the stools had been negative for occult blood. The abdomen became gradually distended but remained soft. Bleeding per rectum continued for about two days. In spite of repeated transfusions his hemoglobin dropped to 65 per cent. A flat plate of the abdomen failed to show evidence of any free air under the diaphragm. Turpentine stupes and small amounts of pituitrin under careful observation were to no avail. He went down-hill steadily and died on the tenth day after admission to the hospital, at the beginning of the fifth week of his illness.

Necropsy Findings. The characteristic intestinal lesions of typhoid fever were found. The lesions ranged from swollen solitary nodules to early necrosis, deep sloughing, and clean ulcers which showed evidence of early healing. The *terminal ileum* was the seat of large Rosenmüller plaques with ulceration. The appearance of the terminal ileum corresponded to that known to occur in the fourth or fifth week of the disease. In view of the association of healing lesions with acute necrotic zones, the presence of a recurrent infection (relapse) was assumed. Severe involvement with an unusual picture of dense infiltration of the mucosal folds was also

found in the rectum. The *lymph nodes* were distinctly enlarged. The *spleen* weighed 690 grams (normal 150 grams) and was soft and red. The *liver* showed numerous typical microscopic typhoid nodular infiltrations with necrosis of liver cells adjacent to the nodules. The spleen contained the same typical nodules, showed erythrocytic phagocytosis and large Rindfleisch typhoid cells. One could see necrosis of the blood vessel walls due to typhoid ulcer extension and associated hemorrhage. The *bone marrow* revealed circular nodules with foci of early necrosis. In the *testes* perivenous nodules were evident. In one area they had produced necrosis of the venous wall and secondary thrombosis.

Case 4. Tuberculosis and Amyloidosis

(From the Pediatric Service of Dr. Bela Schick)

History. (Adm. 415034; P.M. 10579) The patient was a six and one-half year old negress who was in good health until two weeks before admission. At that time she developed severe diffuse abdominal pain and chilliness. During the following two weeks she had a low-grade fever. Three days prior to entrance an increase in the size of her abdomen and puffiness of the face and eyelids were noted. The patient's mother died of pulmonary tuberculosis three years previously. At the time of her mother's demise a Pirquet test and chest X-ray examinations of the patient were negative for tuberculosis. On May 16, 1937, the Mantoux test was four plus and a chest X-ray plate showed enlarged lymph nodes in the right hilus with increased markings in the medial aspect of the right lower lung field.

Examination. On admission the child was acutely ill. Fundi were normal. Examination of the heart and lungs was negative. There were marked abdominal distension, shifting dullness in the flanks, and a distinct fluid wave. The liver edge was palpable three finger-breadths below the costal margin. The edge of the spleen was not felt. There was slight pitting edema of the extremities. The blood pressure was 100 systolic and 70 diastolic.

Laboratory Data. Blood hemoglobin, 68 per cent; red blood cells, 3,400,000; white blood cells, 24,000 (78 per cent polymorphonuclear leucocytes; 16 per cent young polymorphonuclear leucocytes; 4 per cent myelocytes; 2 per cent lymphocytes). Urine showed four plus albumin; microscopically many white and red blood cells and granular casts were revealed. The Schick test was negative. Pirquet test was positive. Preterminally, however, both Mantoux and Pirquet tests became negative. Blood urea nitrogen, 8 mg.; cholesterol, 470 mg. per 100 c.c. Total protein, 5.0 gm.; albumin 1.6; globulin 3.4. A chest X-ray examination showed evidence of atelectasis of the left lower lobe.

Course. Temperature on admission was 101.8°F. and continued to be low-grade in character throughout the patient's stay in the hospital. In view of the large amount of fluid in the abdomen, a diagnostic abdominal puncture was performed and 5 c.c. of grey, turbid fluid was removed which on smear revealed numerous polymorphonuclear leucocytes but no organisms. A paracentesis yielded 30 c.c. of grey, turbid fluid which contained 2,800 cells per cu. mm., of which 90 per cent were mononuclear cells. At this time a blood culture was taken and revealed *Streptococcus hemolyticus*. A simultaneous culture of the abdominal fluid also revealed the presence of *Streptococcus hemolyticus*. Sulfanilamide therapy, 30

grains daily, was therefore started. At this point a flat plate of the abdomen revealed some peculiar radiopaque shadows, the nature of which could not be ascertained. An X-ray examination of the spine, taken on October 18, 1937, showed no abnormality in the bones. However, large calcified masses in the mid-abdomen extending down into the left side of the pelvis were visualized, while a lateral view demonstrated the fact that these masses were mid-abdominal in site. They were thought to represent calcified mesenteric lymph nodes. A Congo red test revealed 75 per cent retention of the dye. Abdominal puncture was again performed and 800 c.c. of yellow-white turbid fluid was evacuated which contained 3,000 cells per cu. mm. Friedlaender bacillus was grown from both blood culture and ascitic fluid. The child was then transfused with 500 c.c. of whole blood. The abdominal fluid continued to reaccumulate rapidly despite repeated paracenteses. Following paracentesis some hard, convoluted, abdominal masses became palpable, particularly in the upper quadrant near the midline. Her general condition steadily became worse, and she assumed a more cachectic appearance. The liver increased in size and the child became more apathetic. There were no meningeal signs manifested at any time. Lumbar puncture revealed the presence of fluid under low pressure with prompt rise following jugular pressure. Neither cells nor organisms were found. The blood urea nitrogen rose to 43 mg. per 100 c.c., the child's breath became uriferous, apathy increased, and death occurred four weeks after admission.

Necropsy Findings. The liver was unusually large for a six year old child and weighed 1200 grams. It was firm, waxy, and pink due to Congo red retention. The kidneys were markedly enlarged and waxy with a conspicuous grey-yellow cast. The glomeruli also showed gross evidence of staining with Congo red. The outstanding gross feature was the striking pale yellow color due to fatty change. The spleen was somewhat enlarged. It was not the sago type of spleen, but rather the diffuse form of amyloid infiltration that is more common in children. Histologic preparations showed amyloid deposits in all the organs which were especially perivascular in location. The tuberculous involvement was found to be exclusively in the lymph nodes. Large right paratracheal lymph nodes were present which disclosed extensive caseation. Some paratracheal lymph nodes were calcified. No primary infect could be found in the lung. The mesenteric lymph nodes were enormously enlarged to the size of apples and showed both caseation and calcification.

Comment. Dr. Klemperer: The more completely calcified paratracheal lymph nodes represent most likely the older tuberculous focus, while the less calcified nodes, although representing a later process, were still in the so-called "secondary" phase of generalization. This phase of late generalization in tuberculosis may exist for a few years.

Dr. Baehr: Infection of the ascitic fluid in nephrosis is most often caused by the pneumococcus. Patients may recover spontaneously from such peritoneal infections, which may later recur due to the same or another type of pneumococcus. The occurrence of ascitic infection in nephrosis in children has been ascribed by some to the presence of a chronic pneumococcal infection of the paranasal sinuses. Dr. Baehr in answer to a question as to the cause of amyloid disease without a suppurative process replied that the amyloidosis is observed not only when there is suppuration in tuberculous cavitations, but that it can be the result of the break-

ing down of the caseating tuberculous lymph nodes. It may be recalled that amyloidosis is also occasionally associated with breaking-down carcinoma or tertiary syphilis; suppuration is not essential in amyloidosis.

Dr. Klempner: Amyloid disease may occur in association with Hodgkin's disease; also, there are infrequent instances of idiopathic amyloidosis.

Reported by M. C. Tyson, M.D.

Wednesday, January 12, 1938

Case 5. Primary Carcinoma of the Liver

(From the Medical Service of Dr. George Baehr)

History (Adm. 417347; P.M. 10613): The patient, a fifty-six year old, Greek-born male, gave a negative past history except for an attack of dengue fever in 1928. No story of alcoholic excess was obtained.

First Admission (October 13 to November 11, 1937). Four weeks before entrance the patient developed an upper respiratory infection lasting several days, which was accompanied by cough with slight expectoration. During this time he also noted increasing abdominal distension and constipation, followed two weeks later by moderate diarrhea. He had no hematemeses, epistaxes, or melena.

Examination. The patient was a well-developed, well-nourished male with slightly icteric sclerae. The heart and lungs were normal. The blood pressure was 130 mm. of mercury systolic and 75 mm. of mercury diastolic. The abdomen was moderately distended. Signs of free fluid were elicited. The radial arteries were moderately sclerotic.

At the time of admission the clinical impression was *cirrhosis of the liver* with ascites due to portal stasis; generalized arteriosclerosis.

Laboratory Data. Saccharin circulation time, 10 seconds, venous pressure, 6 cm. of water; vital capacity, 2,900 c.c. Erythrocyte sedimentation time, two hours and ten minutes. Hemoglobin, 85 per cent; white blood cells, 9,700 (54 per cent polymorphonuclear neutrophils). The urine was negative except for the presence of urobilinogen (1:80) on one occasion. Blood Wassermann reaction, negative; blood cholesterol, 260 mg.; cholesterol ester, 60 mg. per 100 c.c. Icteric index 3, total protein, 6.4 gm. per 100 c.c. (albumin 3.4 gm., globulin 3 gm.). Takata-Ara reaction, 4 plus. Galactose tolerance test gave an excretion of 3.93 gm. An electrocardiogram showed sinus tachycardia with high voltage P waves, slurred QRS and semi-inverted T wave in the third lead. Chest X-ray examination revealed only a moderate bilateral elevation of the diaphragm. Pneumoperitoneum showed a small liver, not definitely nodular, but a definitely enlarged spleen.

Course. Paracenteses shortly after admission yielded 3,500 c.c. of straw-colored fluid which contained 450 cells per cu. mm. (90 per cent monocytes). The abdominal fluid reaccumulated rapidly in spite of diuretics and, accordingly, it was suggested that a variant of the Talma operation be performed. The patient refused, however, and returned home against advice.

Second Admission (Dec. 2 to 9, 1937). During the three weeks following discharge, the abdominal fluid continued to increase. The patient had grown weaker, dyspneic, and anorexic. Three days before entrance, edema of the ankles was noted. Accordingly he returned to the hospital for paracentesis and operation.

Examination. The patient was now emaciated, icteric, appeared chronically ill, and in some distress. The heart was normal. Examination of the lungs revealed diminished breath sounds and medium moist râles at both bases. The abdomen was tense, protuberant, and presented evidences of free fluid. Edema of the lower extremities and scrotum were also noted. The patient was still considered to have *Laennec's cirrhosis*.

Laboratory Data. Blood hemoglobin, 83 per cent with 18,000 white blood cells (84 per cent polymorphonuclear neutrophiles). Van den Bergh test was promptly positive with 3.0 mg. of bilirubin per 100 c.c. Urine contained urobilinogen in the dilution of 1:160. Icteric index, 15. Total blood cholesterol had dropped to 195 mg. per 100 c.c., with only a trace of cholesterol ester.

Course. Paracentesis was again performed. The 3,700 c.c. of clear yellow fluid removed contained 160 white cells per cu. mm. (80 per cent polymorphonuclear neutrophiles). Specific gravity was 1.010. In spite of supportive measures, the patient became weaker, his jaundice deepened, and he lapsed into coma. Death occurred seven days after admission.

Necropsy Findings. The liver weighed 1170 grams. It was distinctly small, firm, and rather distorted in outline. Projecting from the apex of the right lobe and poorly demarcated from the remainder of the liver, was a roughly spherical soft mass about 5 cm. in diameter. It was firmly adherent to the diaphragm. The main surface of the liver had the typical tawny, coarsely nodular appearance of cirrhosis, but the nodule over the right lobe was mottled white with flat, confluent nodules incompletely outlined by interlacing bands of connective tissue from the adjacent cirrhotic portion. Microscopic study of this soft nodule showed the presence of collections of anaplastic cells in an abundant connective tissue stroma which also contained many bile ducts and inflammatory cells. In addition, other areas contained nodules of hyperplastic liver cells which displayed marked atypism. The remainder of the liver presented the typical histological picture of *Laennec's cirrhosis*. The hepatic and portal veins contained tumor thrombi. The lymphatics of the diaphragm were also invaded, and the lungs showed numerous metastatic nodules with tumor tissue in the arteries and lymphatics. A mediastinal node was enlarged to the size of a small plum and completely replaced by tumor tissue. This was adherent to the pericardium but did not invade it. The spleen weighed 235 gm. It was firm and surrounded by chronic perisplenitis. The sectioned surface was light, grayish-pink, and granular. Post mortem skeletal X-ray plates were not revealing.

Comment. *Dr. Klemperer.* This case represents a typical instance of hepatocellular carcinoma with metastases both by blood and lymphatic channels. Such tumors are thought to arise in cirrhosis of the liver, in the areas of compensatory hyperplasia. About 80 per cent of such tumors arise in cirrhotic livers, while the remainder originate in other conditions associated with liver regeneration. In this case, atypism of cells in other hyperplastic areas suggested that they were on the verge of being transformed into frank carcinoma.

Dr. Bachr: A sudden acceleration in the clinical course of a case of cirrhosis, such as the sudden appearance of ascites or of jaundice, is not a reliable indication of carcinomatous transformation. A patient with cirrhosis may develop a superimposed hepatitis with a subsequent course which would be indistinguishable from that due to the occurrence of malignant transformation.

Reported by ARTHUR W. SELIGMANN JR., M.D.

ABSTRACTS

AUTHORS' ABSTRACTS OF PAPERS PUBLISHED ELSEWHERE BY MEMBERS OF THE
MOUNT SINAI HOSPITAL STAFF

Members of the hospital staff and the out-patient department of The Mount Sinai Hospital are invited to submit for publication in this column brief abstracts of their articles appearing in other journals.

The Occurrence and Pathogenesis of Cardiac Hypertrophy in Graves' Disease. C. K. FRIEDBERG and A. R. SOHVAL. Am. Heart J. 13: 599, May 1937.

The hearts in twenty-seven fatal cases of Graves' disease were studied anatomically with particular reference to the occurrence of hypertrophy. By comparison with available standards of normal heart weight, about one-half of these hearts were found to be hypertrophied, corresponding to the incidence generally reported in the literature. However, only two cases (7 per cent) showed cardiac hypertrophy independent of cardiac failure, hypertension, coronary sclerosis or auricular fibrillation, indicating that hypertrophy in uncomplicated Graves' disease is quite uncommon and of slight degree.

The most common explanation of cardiac hypertrophy in Graves' disease is that it results from the increased work of the heart, as indicated by increased cardiac output. It is pointed out, however, that increased cardiac output in Graves' disease is almost always due to tachycardia alone, while the systolic output almost invariably is not elevated. Since dilatation and hypertrophy depend on the increased diastolic tension which would be translated into increased systolic output, there should theoretically be no significant hypertrophy in uncomplicated cases of Graves' disease. When it is present in a given case it indicates that the increased cardiac output in that case was affected not only by tachycardia but also by an increased systolic output.

Contribution Made by Roentgenographic Evidence After the Injection of Iodized Oil. J. H. GLOBUS. Arch. Neurol. & Psychiat. 37: 5, 1077, May 1937.

The formerly prevalent use of intraspinal injections of iodized oil for diagnostic purposes appears to have declined since Davis and his co-workers reported profound alterations in the leptomeninges of dogs that had been subjected to this procedure.

Globus undertook a survey of one hundred and thirty-eight cases in which myelography with iodized poppy-seed oil had been done. In only two cases were there reactions of relative severity immediately following the injection. Sixty-five patients reported for subsequent examinations at intervals up to ten years. In only one instance were there subjective complaints or objective findings which could be regarded as an aftermath of the myelography. In three instances the meninges and spinal cords became available for histologic study but showed no evidence of leptomeningitis.

The evidence presented in this paper indicates that iodology is a useful procedure which helps in the diagnosis of compressing lesions of the spinal cord. It is particularly useful to the surgeon in identifying the precise level of a laminectomy.

The Aortic Commissural Lesion in Rheumatic Fever. LOUIS GROSS AND GERTRUDE SILVERMAN. *Am. J. Path.* 13: 3, 389, May 1937.

This report describes the findings in seventy cases of rheumatic fever segregated into six groups, according to the clinical course taken by the disease. It is shown that a number of inflammatory changes are found in the aortic, root, wedge, annulus, ring, subaortic angle and pericardial mantle which are characteristic of rheumatic fever and, to some extent, reflect the clinical course of the disease. Even when healing takes place the histological characteristics of the commissural lesion afford additional stigmata which are of value in discerning a past rheumatic process. A discussion is given of the pathogenesis of this lesion from which it appears that, even though the original infection may reach the aortic ring through several routes, in most instances the inflammatory granulation tissue passes from the pericardial mantle through the aortic root, wedge and annulus to reach the aortic rings. The latter show a much more flagrant inflammatory process which spreads into the valve leaflets and, probably with the additional factor of trauma caused by the systolic and diastolic movements of the cusps, eventually leads to their agglutination. The possible significance of these findings in relation to the pathogenesis of the so-called congenital bicuspid aortic valve is indicated. A description is also given of the histological and topographical changes taking place during the different age periods in the normal aortic commissural region.

The Determination of Phenol Red in Gastric Contents. F. HOLLANDER, A. PENNER and M. SALTZMAN. *Proc. Soc. Exper. Biol. & Med.* 36: 568, May, 1937.

This is a preliminary report of a new method for the determination of phenol red when used as a dilution indicator in gastric analysis. Previous methods were found unreliable, due to a number of complicating factors. The method described is simple and reliable. The gastric juice containing the phenol red is alkalinized, and bile pigment and protein are both removed by freshly precipitated $\text{Zn}(\text{OH})_2$ without loss of phenol red. The excess Zn is precipitated and the pH simultaneously adjusted by the addition of Na_3PO_4 to a value suitable for colorimetry. At this pH color fading is inappreciable. Beer's law is also applicable in this situation. Results on known solutions of a wide series of dilutions agree to within 1 per cent of the initial concentration of the indicator in the test meal.

Purpura: Classification and Treatment with Special Reference to Treatment with Snake Venom. S. M. PECK, N. ROSENTHAL AND L. ERF. *Arch. Dermat. & Syph.* 35: 831, May 1937.

A classification of purpuric and allied manifestations of the skin and mucous membranes from the clinical and the hematologic standpoint is presented.

Preliminary studies of the histology of purpura from the experimental and the clinical point of view are given.

The value of moccasin snake venom as a diagnostic, prognostic and therapeutic agent in these conditions is discussed.

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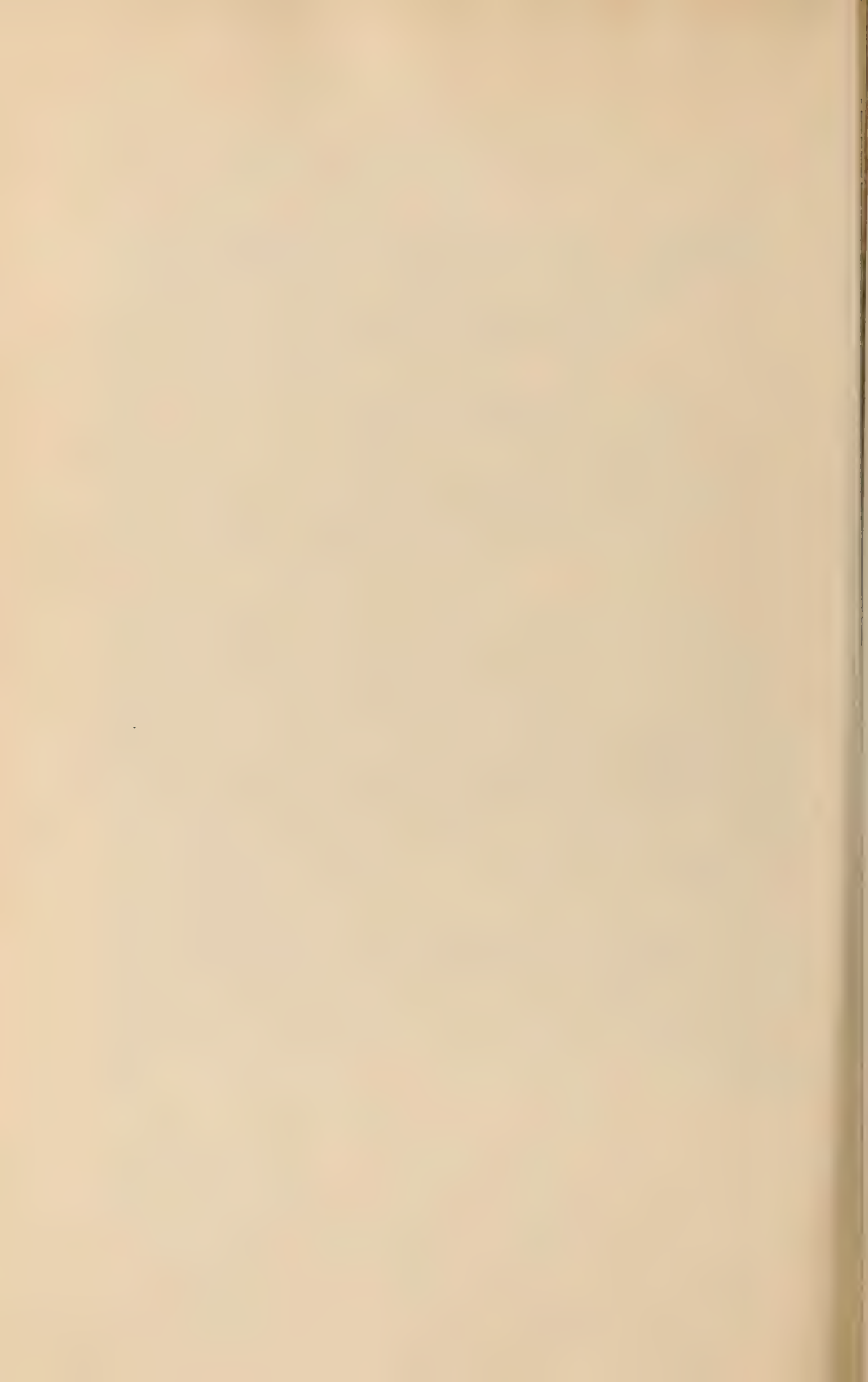
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THE PROBLEM OF HIGH BLOOD PRESSURE IN MAN*

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THE question which will be discussed here is central to the whole problem of human hypertension, namely, the nature of the agent raising the arterial pressure. Until we understand this, no other question can be answered fully and satisfactorily. At the outset it is well to have clearly in mind the possibility that hypertension may originate differently in different clinical conditions. The following discussion will centre round so-called essential hypertension, but acute and chronic nephritis and coarctation of the aorta will be mentioned briefly.

VASOCONSTRICTION

In all the maladies mentioned we may say that the rise in mean arterial pressure is due to vasoconstriction. For the other possible factors, raised cardiac output and increased blood viscosity, have been excluded by direct measurement. We do not yet know whether this vasoconstriction affects equally all vascular areas or affects some territories to a greater extent than others; but the evidence supports the idea that it is more or less uniform. Thus, if vasoconstriction affected some vascular territories more than others we should expect blood to be diverted from vessels that were more, to those that were less, constricted. We might, therefore, expect symptoms of ischaemia to arise from organs, vessels of which were particularly narrow. Such symptoms are uncommon in the early stages, and when they occur in the later or more severe cases, they are, in my opinion, nearly always due to local organic vascular disease. I am dissatisfied with the evidence for the view that so-called hypertensive encephalopathy is due to arterial spasm; hypertensive neuro-retinitis may be, but the question of its origin is complex (21), and the vascular territory small.

The normal bloodflows through the forearm recorded in chronic

*Abstract of a lecture delivered at The Mount Sinai Hospital, April 27th, 1938.

nephritis and essential hypertension by Prinzmetal and Wilson (27) and by myself (22) support the conception of a generalised vasoconstriction, but the measurements perhaps require repetition, in view of the recent demonstration by Grant and Pearson (11) that the forearm plethysmograph used in both sets of observations receives not only blood entering the forearm from the arterial side but also blood returning through the veins from the hand.

On general grounds we would suspect that the vessels chiefly constricted in hypertension would be the small arteries and arterioles where the main vascular resistance lies. This idea is supported by the normal values for capillary pressure found by Ellis and Weiss (2) in essential hypertension and by the normal pressure gradient between brachial and digital arteries found by Oppenheimer and Prinzmetal (19).

THE NATURE OF THE AGENT CONSTRICTING THE VESSELS

It is probable that the disturbance underlying persistent hypertension in man is a more or less uniform narrowing of the small arteries and arterioles. Clearly there are three ways in which such narrowing might arise, namely, from a morphological change in the vessels, or from vasoconstriction of nervous or of chemical origin. It is well recognized that anatomical changes in the small arteries and arterioles are almost invariably present in long-standing cases of hypertension. In both chronic nephritic and essential hypertension, fatty hyaline intimal thickening of these vessels occurs usually in the kidney, and sometimes in other abdominal viscera and in the brain. But these changes are absent, or nearly so, from the large vascular territories of skin and muscle, in which regions the media is usually hypertrophied (3, 4, 5, 16). Most of those who have studied the histology hold that the intimal change in hypertension is insufficiently widely distributed to account *per se* for the rise in pressure, and that the medial change represents a work hypertrophy of the arterial wall analogous to that occurring in the heart. The indication from histological work that the vascular narrowing responsible for raised arterial pressure is a functional rather than an anatomical change is in accord with experimental observations suggesting that in human hypertension the vessels are capable of considerable dilatation. Thus, in the arm the vasodilator responses to circulatory arrest and to heat are of normal range in human hypertension (22, 27). Again, a vasodilator agent such as histamine

produces in chronic nephritis and essential hypertension falls of arterial pressure that are similar to those in normal subjects when allowance is made for different initial pressures (25).

So far in our argument there is fairly general agreement among different workers. The chief cleavage comes when we consider whether the abnormal vasoconstriction responsible for raised arterial pressure is due to over-action of the vasomotor nerves or to a chemical factor. In considering these rival hypotheses it is of great importance that we have a clear conception as to the question at issue. In the normal subject the blood pressure is maintained by the state of contraction or tone of the vessels taken as a whole. Normal vascular tone is undoubtedly in part of nervous origin, as is demonstrated by the vasodilatation which follows section of the sympathetic nerves, and by the profound fall of blood pressure which occurs when the spinal cord is destroyed. Completely denervated vessels are not, however, fully dilated, and it is probable that normal vascular tone is partly also of chemical origin. If we agree that normal vascular tone is partly of nervous and partly of chemical origin then we must assume that vascular tone in hypertension has at least these two components and what we have to find out is which of the two is abnormal. To prove that hypertension is due to vasoconstriction of nervous origin, it is clearly not enough to demonstrate vasomotor nervous tone; it must be shown that this is excessive. Similarly, to demonstrate the chemical origin of hypertension, an increase must be shown in the chemical component of vascular tone.

THE EVIDENCE FOR THE NERVOUS HYPOTHESIS

With these considerations in mind let us examine the evidence that has been advanced for the nervous hypothesis. One of the most complete hypotheses for the origin of hypertension was that due originally to Hering (13) and later supported by Mies (17) and Regniers (30), and which supposed that the raised pressure was due to interference with the carotid sinus and aortic reflexes. This hypothesis is now generally abandoned, since it has been demonstrated that the carotid sinus reflex functions in hypertension (7, 25), and since the hypertension produced in animals by section of the carotid sinus and depressor nerves differs considerably from that found in man. A second hypothesis put forward by Raab (29) and others was that essential hypertension was due to ischaemia of the medulla and consequent increased irritability of the vasomotor

centre. Raab's evidence has been partly, though not wholly, controverted, but his idea has won no general acceptance chiefly because the respiratory centre seems much more sensitive than the vasomotor centre to changes in the gas content of the blood.

Those who now uphold the nervous hypothesis do not specify the way in which over-activity of the vasomotor nerves is brought about. They rely for their support mainly on the evidence derived from the cold pressor test and from the effects of dividing the sympathetic supply to the abdominal viscera. Hines and Brown (15) consider that an unusually large rise of blood pressure in response to immersing one hand in water at 4°C. is characteristic of essential hypertension; a few subjects with normal blood pressure may show an equally large response, but these usually have a family history of hypertension and are regarded as potential or future sufferers from the disease. Hines (1937-8) has recently emphasized the significance of this test by showing that in families having a large response to cold hypertension is common, while in those having a small response hypertension does not occur. On the other hand, Kissin and I (Pickering and Kissin, 1935-6) found that a large response to cold was not peculiar to essential hypertension, being occasionally absent in the condition and sometimes present in subjects of comparable age with normal pressures and no family history of the disease; our series of patients was, however, small. Whether or not an exaggerated response to cold is peculiar to essential hypertension is a question of fact which will ultimately be decided by observation; purely for the purposes of argument, let us assume that it is so and consider its interpretation. The rise of blood pressure in response to cold is almost certainly due chiefly to vasoconstriction of nervous origin; an unusually large rise may be due to an enhanced irritability of the vasomotor center, as Hines and Brown suppose, but it might also be due to enhanced irritability of the peripheral vessels, or to a diminished sensitivity of the proprioceptive mechanisms regulating blood pressure, which would allow an unusually great change in pressure to occur. As evidence for the nervous origin of essential hypertension the cold pressor test is thus by no means unequivocal.

In considering operations for denervating the splanchnic area it is important to distinguish the therapeutic from the scientific implications of the results obtained. The operations, largely introduced by Adson and his colleagues, are of two kinds, section of the anterior spinal roots from about the sixth thoracic to the second lumbar, and

section of the major and minor splanchnic nerves above or below the diaphragm with removal of the adjacent sympathetic ganglia; and there seems to be no doubt that they are successful as therapeutic ventures in certain cases. These two operations seem to produce similar effects on the arterial blood pressure in essential hypertensives (1, 6, 20); in some patients the fall of blood pressure is profound and persistent; in most, a considerable fall is ultimately followed by a return to approximately the pre-operative level; and in a few the blood pressure is unaltered. The variability of the results obtained and the insufficiency of the control series makes the interpretation of these results extremely difficult. From general considerations, and from the effects of similar operations on normal dogs (12) and on dogs with hypertension originating chemically from renal ischaemia (10), we may interpret those results in which a variable post-operative fall is followed by a return to the pre-operative level of arterial pressure as meaning no more than that normal vasomotor nervous tone has been removed from the splanchnic area. In those instances where the blood pressure returns permanently to normal this explanation may be insufficient, and we may suspect either that the hypertension was due to excessive vasomotor nervous tone, or that splanchnic denervation has produced its effects in an indirect manner, such as by increasing the bloodflow through a previously partly ischaemic kidney. If this latter explanation were correct we should expect similar results to follow simple renal denervation; but this operation has not yet been performed on a sufficiently extensive scale.

THE EVIDENCE FOR THE CHEMICAL THEORY

The interpretation of changes in blood pressure due to experimental interference is rendered hazardous by the complexity of the factors involved. It occurred simultaneously and independently to Prinzmetal and Wilson (27), and to me, (22), that the question of the nervous or chemical origin of hypertension could be settled by the following simple experiment. In any organ the bloodflow is proportional to the perfusing pressure divided by the resistance offered by the vessels. In persistent hypertension, the bloodflow through the upper extremity seems to be normal, that is to say the increased perfusing pressure is balanced by increased vascular resistance. Supposing that we completely remove vasomotor nervous tone from the vessels of the hand, then if the abnormal factor constricting the vessels is nervous, it should disappear under these

circumstances and bloodflow through the hand would be greater in the hypertensive than in the normal subject since increased arterial pressure would no longer be balanced by increased resistance. If, however, the abnormal factor is not nervous then it will not disappear with the removal of vasomotor nervous tone; increased blood pressure will still be balanced by increased resistance and in hypertensive patients bloodflow may be no greater than in normal subjects under comparable circumstances. To measure bloodflow Prinzmetal and Wilson used Hewlett and Van Zwaluwenberg's plethysmographic method with Lewis and Grant's forearm plethysmograph, reference to which has already been made. I used Stewart's calorimetric method on the hand as an index of its bloodflow, removing vasomotor nervous tone from the hand by raising the body temperature. Evidence was obtained that the calorimetric method provided a reliable index of bloodflow and that the degree of body warming employed was sufficient entirely to remove vasoconstrictor nervous tone from the hand. As regards essential, malignant, and chronic nephritic hypertension we agreed in finding normal bloodflows after removing vasomotor nervous tone. In these conditions therefore, the experiment suggests that the abnormal factor in the peripheral resistance is not nervous and is presumably chemical in origin. In coarctation, Prinzmetal and Wilson found abnormally large flows and I found normal flows. Several possible reasons for this discrepancy may be advanced, but these have not as yet been investigated. I was forced to conclude that the increased resistance in the upper limb in coarctation was also of non-nervous origin. On the other hand in four of six cases of acute nephritis in the hypertensive phase I did find increased flows through the hand from which vasomotor nervous tone had been removed, and the increase was of the order to be expected from a simple increase in arterial pressure. In these cases, therefore, there was no evidence of non-nervous vasoconstriction in the hand during the hypertensive phase, a result consistent with the view that hypertension is due to vasoconstriction of nervous origin. As yet no pressor reflex mechanism has been demonstrated from the kidney.

To return to essential hypertension, the suggestion from these experiments is that the raised blood pressure is of chemical origin. A pressor substance has frequently been sought in the blood but experiments in which extracts or ultrafiltrates of blood are tested and found negative are all open to the interpretation that the pressor

substance was present in the discarded fraction. Accordingly, I measured the changes of blood pressure produced in anaemic patients receiving blood from normal donors and donors with essential hypertension (23). No appreciable rises of blood pressure occurred even when 600 c.c. of blood from a hypertensive donor were introduced in six minutes. Prinzmetal, Friedman, and Rosenthal (28) made similar observations in malignant hypertension and found no pressor response from transfusion of as much as 2300 c.c. of blood from a hypertensive donor. It is evident therefore, that if a circulating pressor substance exists in benign and malignant hypertension, it is present in surprisingly small quantities. If the chemical theory is correct, then the agent would appear to be one which is relatively stable in the body and which is fixed by the vessels on which it acts. The strongest clues point to the kidney as a possible source of such a pressor substance. Thus, in chronic nephritis there are many reasons for supposing that the kidney is the seat of the primary disturbance which results in hypertension. Again, Goldblatt (8) has shown that a persistent hypertension, which resembles essential hypertension in the maintenance of a relatively normal renal function, may be produced in the dog by constricting the renal arteries. More recently he has shown that when the constriction is severe, albuminuric retinitis, arteriolar necroses and renal failure occur as they do in the malignant phase of human hypertension (9). Wilson and I (32) have also reported the occurrence of widespread necrotising arteriolar lesions in rabbits with severe hypertension from renal artery constriction. From these observations there is no doubt that something very similar to the benign and malignant phase of essential hypertension may be produced in animals by renal artery constriction. And there is little doubt that this experimental hypertension is chemical and not nervous in origin. Finally, Moritz and Oldt (18) have produced histological evidence suggesting that renal arteriolosclerosis is the primary lesion in essential hypertension.

The question arises: are essential and chronic nephritic human hypertension due to the release into the circulation of a chemical substance by the kidneys, and perhaps its subsequent fixation by the vessels? We know that a protein-like pressor substance is a normal constituent of the renal cortex. It was described in 1898 by Tigerstedt and Bergman (31). The failure of many workers to find it is probably due chiefly to its action being reduced or abolished by anaesthetics (26). Whether this substance is concerned in the

production of experimental or human hypertension is a question which it is as yet unprofitable to discuss, but there is no doubt that evidence for or against the hypothesis will accumulate in the near future.

In this account I have attempted to develop a line of thought rather than to prove a scientific hypothesis. Proof will not come until we can demonstrate in detail the mechanism whereby the arterial blood pressure is raised in man. But in looking for such a mechanism we must have some guide, and it seems to me that on the available evidence the most profitable line to explore is that which I have tried to indicate here.

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MASSIVE CEREBRAL HEMORRHAGE^{1,2}

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ITS ANTECEDENT AND PRECIPITATING FACTORS

UNDER the term of massive cerebral or, better, spontaneous intracerebral hemorrhage there are to be considered only those instances in which a sudden and explosive occurrence results in the extravasation of a large mass of fluid blood into a concurrently or previously disorganized area of brain tissue. The term suggested not only indicates the massive form of the bleeding, not only identifies the location of the bleeding as being in the substance of the brain itself, but also suggests the spontaneous and explosive character of the bleeding. Moreover, it points to its independence of external factors, particularly that of trauma. It also permits of the assumption that the precipitating cause of such a vascular eruption is linked up with some preexisting factors or conditions inherent to the brain substance and its vascular apparatus. The term, besides its descriptive qualities, has the additional value of imposing some restrictions in its application to cerebral bleeding. It excludes from its category those extravasations in which the accumulated blood is little more than a conglomerate of small hemorrhages, often microscopic and petechial in character. It also excludes hemorrhages which, though massive in extent, arise in the subarachnoid, subdural or other extracerebral locations, and, as such, are not part of a true intracerebral hemorrhage.

Before the antecedent and precipitating factors of this condition are brought under discussion, it would be appropriate to consider some of the views held by earlier investigators. Rouchoux (1), of course, is to be mentioned first. His name is a familiar one whenever the pathogenesis of cerebral hemorrhage, or "hemorrhagic apoplexy,"

¹ Read before the meeting of the Association for Research in Nervous and Mental Disease, December 28, 1937.

² From the Laboratories, Medical and Neurological Services of The Mount Sinai Hospital.

as it was known before, is discussed. He is credited with the popularization of the concept of "prehemorrhagic brain softening," an observation which is said to have been made a few years earlier by Pariset (2). In the opinion of Rouchoux, cerebral, hemorrhagic apoplexy is always preceded by a gradual and clinically unrecognized alteration of brain substance, resulting in the reduction of its cohesive properties. This, in his opinion, paves the way for the rupture of cerebral blood vessels which, while still subjected to normal pressure, break because of the softer consistency of the surrounding tissue and cause extravasation. He discovered in a large number of instances a narrow zone of altered tissue about apoplectic cavities. The tissue was soft, semi-fluid in make-up, and yellowish in color. Moreover, he observed some instances in which a break in the blood vessel causing the hemorrhage was readily detected within such cavities. He was thus led to the conclusion that the preexistent reduction in the consistency of brain tissue was responsible for the series of events resulting in fatal hemorrhage. In an attempt to evaluate more carefully the importance of the preexisting stage of softening, he himself propounded the question as to whether this alteration in the brain consistence could not be the *result* of the hemorrhage rather than its precursor. He answered his own question in the negative, for he believed that if one is to assume that such a condition is provoked by the hemorrhage which has had an existence of a day or more, then, when death occurs within a very brief period after hemorrhage has set in, such a condition should not be encountered. This, however, does not obtain—the zone of softening is found to be present, no matter how soon death intervenes.

The view of Rouchoux was accepted by many in full, by others with such modifications as would conform with their own observations. Thus Durand-Fardel (3), who also was of the opinion that the pre-existence of such a cavity favored cerebral hemorrhage, ascribed the existence of such defects to a condition which he named "interstitial atrophy of the brain." His conclusions were based on the presence of a large number of small excavations about areas of cerebral hemorrhage or in brains in which hemorrhage was impending. Todd (4), an English investigator, was also in sympathy with the concept of Rouchoux and had attempted to bring it into correlation with some of his own clinical observations. He projected the view that cerebral hemorrhage had its phases and that each phase presented a fairly character-

istic clinical picture. Thus the patient with the hemorrhage confined to the brain substance is likely to display one set of clinical manifestations while, when the blood escapes from the hemorrhagic focus into the adjacent cavities or spaces, there is an advent of new signs and symptoms. In striking contrast to these views, Charcot and Bouchard (5), who objected strongly to the concept of Rouchoux, brought forward their own explanation for cerebral hemorrhage. It made a deep impression upon their contemporaries and remained fixed in the minds of many who followed them, for a long time. Charcot and Bouchard, in opposing the concept of a preexisting area of softening, claimed that not sufficient proof had been advanced in support of that idea which, moreover, was in conflict with their own findings. In their, now historical, monograph they eliminated increased tension in cerebral vessels, as well as the reduction in the consistency of the brain at the point of bleeding, as factors in the causation of cerebral hemorrhage. They brought forward their own observations, which pointed to the existence of small sacular enlargements of vessels floating in the blood of a hemorrhagic area in practically every case of cerebral hemorrhage examined by them. In some instances they found these vascular anomalies also on the surface of the brain in parts in which hemorrhage had not yet taken place. They named these multiple and rather minute vascular expansions "miliary aneurysms" and, because of the uniformity and the consistency with which they could detect them in apoplectic cerebral bleeding, they assigned to them a place of utmost importance in the etiology of cerebral hemorrhage. This concept acquired many adherents and became a tradition in medical literature. Nevertheless, it was destined for radical revision on coming under the scrutiny of critical anatomists. Thus Hasse (6) found that the aneurysms were not primary vascular defects and, like Virchow (7), reached conclusions which pointed to the likelihood that they were secondary manifestations of diseased blood vessels. This was also the opinion of Eppinger (8). It was now the consensus of opinion that these local expansions of small vascular branches were "false aneurysms," mainly in the nature of dissecting aneurysms. Rupture of such aneurysms was held responsible for cerebral hemorrhage. More recently Pick (9), Osler (10), and Ellis (11) have all reached similar conclusions.

Despite all these studies and discussions, the problem of cerebral hemorrhage has not been accepted as solved; it has continued to

intrigue the anatomist and the clinician alike. More evidence was demanded to prove that vessels, though altered in structure, but embedded in the substance of the brain, may, under certain conditions, rupture and cause massive hemorrhage.²

Thus the pendulum swung again in favor of the prehemorrhagic stage of softening of Rouchoux. But, again, facts were needed concerning the probable cause of such a pathological process. Rosenblath (12), resting on the studies of Baer (13) and his own findings that in a large number of cases of cerebral hemorrhage there is coexistent and advanced renal disease, was tempted to postulate the probable elaboration and circulation of an enzyme which, on lodging in the brain, might lead to autolysis of nervous tissue in some brain territory, thus creating an area of softening predisposed to cerebral hemorrhage. But this purely hypothetical suggestion could not be accepted. The belief in the existence of this prehemorrhagic stage continued, nevertheless, to find new adherents. Among them was Westphal (14), who, cognizant of the fact that manifestations of cerebral dysfunction may occur without subsequently discernible alterations in the brain, suggested that such disturbances could only be attributed to functional deviations in its vascular mechanism. He advanced the idea that *angiospasm*, a sudden narrowing of one or more cerebral vessels, was the probable cause of local ischemia. This, in his belief, when recurring or continuing over a period of time, led to the formation of zones of softening. With the wearing off of the spasm the vessel reopened and was now subject to pressure of the returned blood and no longer supported by a wall of firm brain tissue, but surrounded by a zone of disorganized tissue of lessened cohesion and lowered resistance. This new factor, when added to the inherent defect in the vessel, resulted in hemorrhage.

More recently there appeared the valuable and the often quoted work of Schwartz (15). In this very extensive study of what he chooses to call "apoplectic damage to the brain," he brings under one heading lesions which heretofore bore separate designations indicative of anatomical and clinical distinctions. In gathering under the same heading the embolic, local arteriosclerotic and hypertensive hemor-

² This in spite of the fact that, with the general intracranial pressure being less than 200 mm. of water (average estimate) and with the intra-arterial pressure being well above 1200 mm. of water in most of the patients, rupture of a vessel may lead to massive cerebral hemorrhage even in the normal brain.

rhagic lesions, he is inclined to regard them as somewhat varied morphological expressions of a common physio-pathologic process. In support of this thesis he employs the experimental observations and the theoretical considerations of Ricker (16). The central idea in that theory is that the injury to tissue is always secondary to local circulatory disturbances and that the latter may result from any form of stimulus or irritant mediated by the nervous mechanism of the affected blood vessels. The latter not only transmits the stimulus and its effects to the tissue at the point of application, but allows its propagation by the nervous extensions to other parts and branchings of the affected vascular trunk. The degree of injury, thus induced, depends upon the intensity and duration of the stimulus, no matter what its source or character. Three stages are recognized: (*a*) the stage of fluxion; (*b*) that of ischemia and (*c*) finally, one of stasis. It is during this last stage that the active diapedesis and extravasation take place, and, under certain circumstances, hemorrhage results.

Utilizing this theory, Schwartz speculates on the cause of cerebral hemorrhage and advances his thesis that the following set of events is the main factor in the production of apoplectic hemorrhage: An injurious stimulus (nervous or physical), brought to bear upon a vessel in certain more or less regularly selected parts of the brain, causes physiological changes in the larger vascular trunks. Through propagation of that stimulus by way of the neurovascular network to the smaller peripheral subdivisions, circulatory disturbances are initiated in the related parts of the brain. These disturbances at first take the form of stasis and are subsequently amplified by extravasations into the perivascular spaces. Concurrently nutritional changes begin to develop, causing zones of rarefaction and softening in the affected areas of the brain. The continued effect of the stimulus, provoked, among other factors, by the continued impact of the pulsating blood stream with the vessel wall, not only intensifies the local effects, but allows the transmission of this injurious impulse by way of the neurovascular mechanism to an increasingly widening sphere of related parts of the brain. Numerous petechial hemorrhages occur in the affected areas; these fuse and in this way give rise to the larger, so-called, massive hemorrhage.

Other salient points in the work of Schwartz are (*a*) his failure to find ruptured blood vessels in a single case of cerebral hemorrhage; (*b*) the uniformity in the anatomical distribution of the hemorrhagic

lesion; (c) the presence of vascular lesions with the character of hematomata in the adventitial walls, simulating by appearance the ampular miliary aneurysms of Charcot and Bouchard; (d) the failure to find closed (thrombosed) blood vessels in hypertensive cerebral hemorrhage; and (e) the greater regularity with which hypertensive cerebral hemorrhage occurs in areas which were the sites of previous injury.

Some of these observations cannot be corroborated, while others may be given interpretations which are not in harmony with those advanced by Schwartz. All this will become obvious when I present my own observations and conclusions.

In a previous contribution (17), Strauss and I presented our views on the pathogenesis of massive cerebral hemorrhage and suggested that a prehemorrhagic stage of softening antedates the abrupt vascular explosion. Presumption of the existence of such a prehemorrhagic lesion was based on some clinical data and was supported by what seemed to be convincing anatomical observations. The latter, however, were made on only eight cases. It was, nevertheless, recognized then, as now, that the prehemorrhagic phase of softening frequently escapes clinical recognition. This is probably due to the mildness of the lesion, causing a disturbance in function so minimal as to be undetected on objective study. In some instances quite obvious, though transient, signs and symptoms probably are not given their full significance.

Recently more ample material became available for study and made it possible to put to test the previous observations and conclusions and to evaluate them in the light of the concepts presented by other investigators. The investigation was carried out upon an additional twenty-eight cases of cerebral hemorrhage which, with the previously studied eight cases, fall into the following categories.

Group I. Cases of cerebral hemorrhage in which a clinical history indicated the preëxistence of focal vascular disease of the brain.

Group II. Cases of cerebral hemorrhage in which the clinical history justified the assumption of the existence of vascular disease of the brain, antedating the fatal hemorrhage, without, however, displaying evidence of an earlier focal cerebral disorganization.

Group III. Cases of cerebral hemorrhage in which no history of a preëxisting focal or diffuse cerebral vascular disease was obtained, the latter being revealed only at post mortem examination.

Group IV. Case in which a ruptured aneurysm of a large vessel at the base of the brain was followed by hemorrhage, with blood entering a large preëxisting cavity in the brain substance, the latter presumably caused by the aneurysmal pressure and concomitant hemorrhage into the subarachnoid space.

The study was extended beyond the thirty-three cases to include a large number of cases which showed the preëxistence of advanced vascular disease of the brain, but which failed to terminate in cerebral hemorrhage.

CLINICAL OBSERVATIONS

In the survey of this material particular attention was paid to clinical manifestations antecedent to the fatal hemorrhage, such as cardiovascular and renal disorders; to clinical evidence of previous occurrence of episodes of focal or general cerebral involvement; to the clinical features characterizing the onset of the fatal illness; and to the character of the cerebrospinal fluid during the various stages of the terminal illness.

Hypertension. In twenty-nine out of the thirty-three cases there was a history of hypertension existing for various periods of time preceding the fatal illness. In some of the patients, in whom a reliable anamnesis could not be obtained, the elevated blood pressure at the time of admission to the hospital was accepted as an indicator of its preëxistence. In twenty-seven of the cases both the systolic and diastolic pressures were high. In very few cases was the diastolic pressure only slightly above 100; in only one instance was it below 100 (table 1).

Hypertrophy of the heart. In twenty-one of the thirty-three cases full autopsies were performed. In all but two of these hypertrophy of the left ventricle was found. In only two the heart was of normal size, but the muscle was rather flabby. These are the two cases in which the diastolic pressure was relatively low. In a large number of the cases in which no full autopsy was performed, the heart was found to be enlarged, on clinical examination.

Renal lesions. Here again, in all but one of the instances in which autopsies were performed, the kidneys displayed changes of arteriosclerosis in various stages of development. In some in which no autopsy was obtained the urinalysis disclosed albumin and casts. This was of little service in establishing a renal lesion.

TABLE 1

	POST MORTEM	NUMBER	SEX	AGE	TENSION	HEART	KIDNEYS	PERIPHERAL VESSELS	PREVIOUS CONDITIONS	DURATION OF FATAL ILLNESS	REMARKS
1	Brain only	3749	F	58 yr.	195/100	Enlarged	Albumin and casts in urine	Not recorded	Frequent severe headache, dyspnea, edema, nocturia	7 days	
2	Brain only	4719	F	25	195/125 250/170	No record	Chronic renal disease	Not recorded	Recurrent attacks of increased intraventricular pressure with focal signs		Died following craniotomy
3	Brain only	4802	M	68	230/90	No record	No record	General arteriosclerosis		Few hours	
4	Brain only	4949	F	45	No record	No record	No record	Not recorded	Hemiplegia followed by improvement	18 days	Ventriculography negative; cerebrospinal fluid pressure 390 mm. of H ₂ O
5	Brain only	4978	F	42	190/140	No record	Negative findings	Not recorded	Hypertension for several years	Death sudden	Death after ventriculography
6	Full autopsy	4982	M	62	190/120	Large, fibrous	Nephrosclerosis	General arteriosclerosis	Attack with loss of consciousness followed by recovery and recurrence	48 hours	Blood and cerebrospinal fluid positive Wassermann
7	Full autopsy	5840	M	63	200/?	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis		Few hours	Cerebrospinal fluid bloody
8	Full autopsy	6194	F	56	210/150	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Attack of hemiplegia	2 hours	Cerebrospinal fluid bloody

9	Full autopsy	6260	F	46	250/160	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Mental alterations	5 days	Cerebrospinal fluid clear at first
10	Full autopsy	6900	M	36	220/148	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Hypertension and attack of hemiplegia	Shortly after admission	
11	Full autopsy	7126	F	41	190/?	Hypertrophy of left ventricle	Nephrosclerosis	No record	Attack of loss of consciousness	1 day	Blood Wassermann positive; cerebrospinal fluid 110 red blood cells
12	Full autopsy	7409	F	38	224/146 270/164	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Focal signs	6 days	
13	Full autopsy	7660	F	57	250/158	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Hypertension 10 years	15 days	Uremia
14	Full autopsy	7835	F	69	Not recorded	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Hypertension 6 weeks	1 day	Cerebrospinal fluid bloody, 400 mm. H ₂ O pressure
15	Full autopsy	7852	F	64	150/52	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Hypertension. Diabetes 5 years. Hemiplegia	1 day	Diabetic coma
16	Full autopsy	8168	F	52	150/100	Dilated flabby heart	Not involved	Moderate arteriosclerosis	Mental changes for two weeks	3 days	Cerebrospinal fluid bloody
17	Brain only	7960	F	55	220/20	No record	No record	No record	Hypertension	12 hours	Pontine hemorrhage
18	Full autopsy	7899	M	57	300/140	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Hypertension	2 hours	

TABLE 1—*Continued*

	POST MORTEM	NUMBER	SEX	AGE	TENSION	HEART	KIDNEYS	PERIPHERAL VESSELS	PREVIOUS CONDITIONS	DURATION OF FATAL ILLNESS	REMARKS
19	Brain only	X 208	M	39½-45	170-105	No record	No record	No record	Hemiplegia 4 years	Death sudden	Death following craniotomy
20	Full autopsy	8497	M	42	200-128	Hypertrophy of left ventricle	Nephrosclerosis	General arteriosclerosis	Hypertension 14 years	1 hour	
21	Full autopsy	8549	F	70	200-100	No enlargement	Nephrosclerosis	General arteriosclerosis	Hypertension 2 years	4 days	
22	Brain only	8633	M	49	220-150	Enlarged	Albumin and casts in urine	No record	Hypertension 5 months	9 weeks	Cerebrospinal fluid bloody
23	Brain only	9345	F	64	170-100	Enlarged	Nephrosclerosis	No record	Hypertension 7 months	12 hours	
24	Full autopsy	9562	M	40	300-205	Large (giant) heart	Nephrosclerosis	General arteriosclerosis	Hypertension for years	17 days	
25	Full autopsy	9779	M	42	280-160	Large	Nephrosclerosis	General arteriosclerosis	Hypertension 5 years. Hemiplegia 5 weeks	1 day	Cerebrospinal fluid bloody
26	Full autopsy	9822	M	30	210-180-260-150	General hypertrophy	Nephrocirrhosis	General arteriosclerosis	Hypertension 3 years	Few hours	Cerebrospinal fluid bloody
27	Brain only	9932	F	42	210-95	No enlargement	No pathological findings	No record	Hypertension 2 years. Previous attack 5 weeks	1 hour	Cerebrospinal fluid bloody
28	Full autopsy	10039	M	53	250-165	General hypertrophy	Nephrocirrhosis	General arteriosclerosis	Headache, dyspnea, blurred vision 4 years	11 days	

29	Full autopsy	10051	M	52	No record	General hypertrophy	Moderate nephropathy	General arteriosclerosis	Hypertension 7 years. Previous attack with recovery 2 years	1/2 hour	Cerebrospinal fluid bloody
30	Brain only	10103	F	42	176/115	Markedly enlarged	No record	No obvious changes	Hypertension 2 years. Transient loss of consciousness 5 months	1 day	Cerebrospinal fluid bloody
31	Full autopsy	10148	M	54	190/160	Hypertrophy of left ventricle	Parenchymal changes	General arteriosclerosis	Hypertension for some time	Few hours	Cerebrospinal fluid bloody
32	Brain only	10263	M	37	120/84 170/88	Not enlarged	No findings	No obvious changes	3 previous admissions with picture of subarachnoid hemorrhage	Few hours	Cerebrospinal fluid bloody
33	Full autopsy	10489	F	60	254/136	General hypertrophy	Nephro-cirrhosis	General arteriosclerosis	Hypertension 10 years	4 days	

Generalized arteriosclerosis. In all of the cases that came to autopsy the aorta and other large vessels showed advanced stages of arteriosclerosis. In some who did not have a full autopsy, the clinical examination disclosed hardening of the radial vessels.

Previous attacks. In twelve of the thirty-three cases a history of previous attacks was obtained. These occurred on occasions antedating the final illness by a period of three days to four weeks. Some of the attacks were a transient loss of consciousness; others were a transient or permanent paralysis. It is significant that in the cases showing previous paralysis the fatal hemorrhage occurred in an area of the brain localized clinically as responsible for the symptoms.

Onset of fatal hemorrhage. In all of the cases studied the onset of the terminal illness was precipitate. The abrupt occurrence was not preceded by any emotional outburst of the patient, by any unusual activity, or by any violence to the patient. In fact, in the majority of cases there was practically no warning of the impending catastrophe. The attack was commonly ushered in by a sudden loss of consciousness, collapse, and the appearance of focal signs. The focal manifestations were mainly in the nature of paralysis and, wherever a previous attack had occurred, the paralysis affected the part of the body involved in the earlier episode. In only two cases were there prodromal signs and symptoms which preceded the attacks by a few hours.

Trauma. In none of the cases was there a history of violence to the head or any other form of violent action which could be regarded as having a direct or indirect bearing upon the condition of the brain, its vascular structures or the blood stream. In many instances the attack had its onset at night with the patient in bed, or during the day with the patient engaged in usual activity. Only in two instances was a direct trauma, the intrusion of the surgeon's aspiration needle into the brain, the cause of a fatal hemorrhage in an already softened part of the brain. In these two instances alone was there any difficulty in diagnosis, and tumor cerebri was seriously considered as a probability. In both of these cases intracranial exploration was undertaken with disastrous results. The exploring needle, used to detect the presence and location of tumor, provoked hemorrhage into an area of softened brain. This caused a sharp change in the patient's condition which was followed rapidly by death.

Terminal course. With but few exceptions the patients reached the

hospital within a few hours after the onset of the fatal illness. Eighteen of these patients died from within one-half hour to twelve hours after admission to the hospital. Seven died on the second to the sixty-third day in the hospital. In the latter instances, as will be apparent from the report on the cerebrospinal fluid findings, the hemorrhage apparently had not yet occurred or was confined to the brain substance at the time the patients entered the hospital and did not break into the ventricular or the subarachnoid space until shortly before the fatal issue. A few of these at first gave evidence of improvement, and there was a transient return of consciousness, followed by a sudden loss of consciousness marking the final stage in the disease process.

The cerebrospinal fluid. In eleven instances the fluid obtained was frankly bloody. This was usually in those cases which died soon after admission, the lumbar puncture being performed shortly before death because of a grave change in the condition of the patient.

ANATOMICAL FINDINGS

The hemorrhagic cavity. In every case an area of completely disintegrated tissue was filled with a mass of partly coagulated blood. With the blood undisturbed, it could often be observed that the cavity containing it was communicating with some part of the adjoining ventricle through a defect in a narrow necrotic zone of tissue intervening between the two spaces (fig. 1). Under these circumstances all the subdivisions of the ventricular system were usually found to be flooded with blood. In several instances the hemorrhagic cavity was found communicating with the subarachnoid space through a break in the thin and softened layer of cortex overlying the hemorrhage (fig. 2). In other cases the wall of the hemorrhagic cavity was found defective on both the ventricular and the meningeal sides (fig. 3), with the blood filling the ventricles and spreading through the subarachnoid space.

On removing the blood with the aid of a gentle stream of running water, rigid, tortuous, friable and, in places, fragmented blood vessels were brought in view. They appeared to be free and, for the most part, detached from brain tissue, bridging over the hemorrhagic cavity (fig. 4). Such vessels could also be disclosed in the hemorrhagic cavities of brains which were previously hardened in formalin, by exposing the latter to the macerating effect of a mixture of water

and peroxide of hydrogen. These vessels, when detached and examined, unsectioned, under the microscope, were found to be badly damaged. They displayed extreme irregularity in contour and reduc-

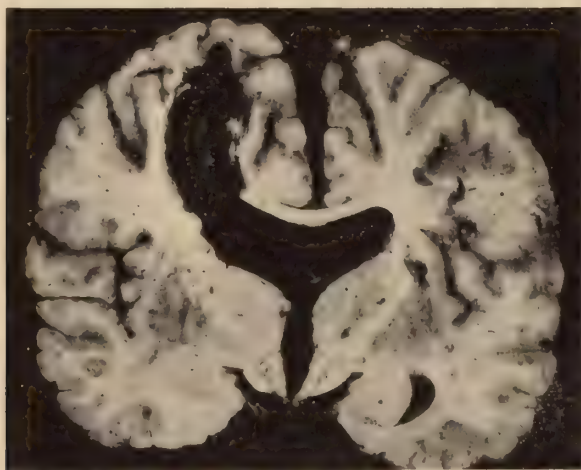


FIG. 1. Massive hemorrhage, emptying into the adjoining ventricle and spreading through the ventricular system.

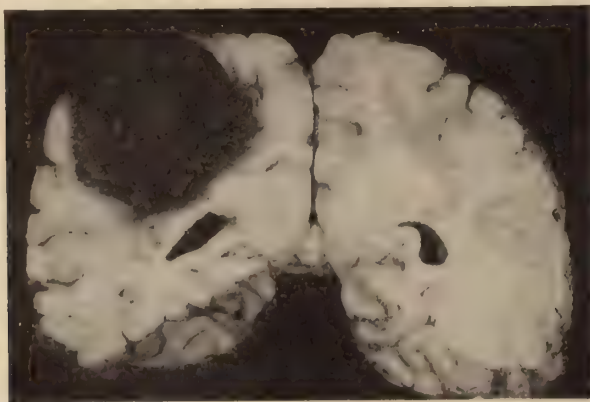


FIG. 2. Massive hemorrhage, spreading into the overlying subarachnoid space.

tion of their lumen, as detected by variations in transparency. The degree of degeneration these vessels had undergone could be best recognized on studying them in serially cut celloidin preparations of

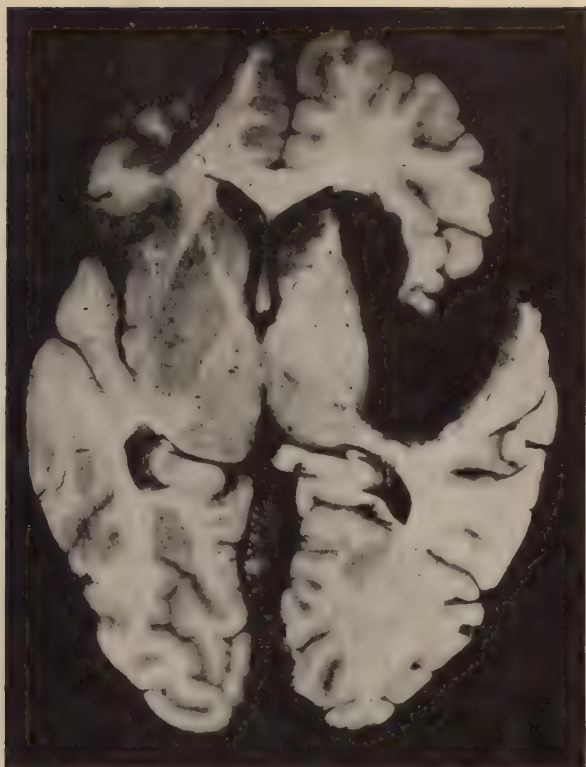


FIG. 3. Massive hemorrhage, emptying into the adjoining ventricle and the overlying subarachnoid space.

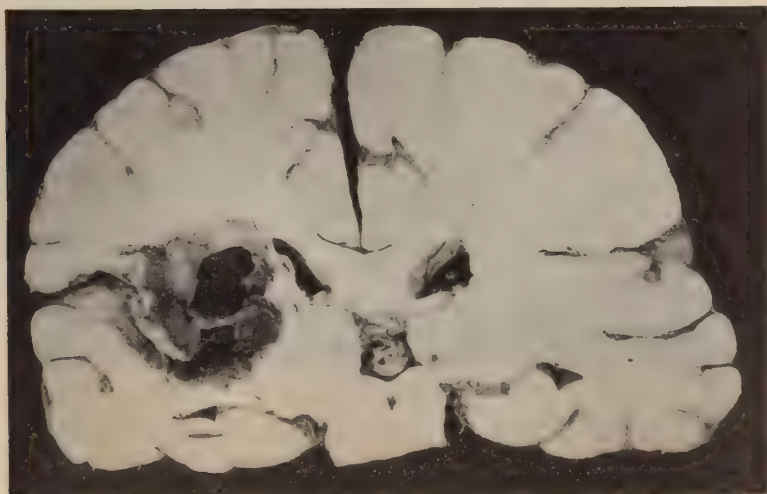


FIG. 4. Hemorrhagic cavity displaying an exposed blood vessel

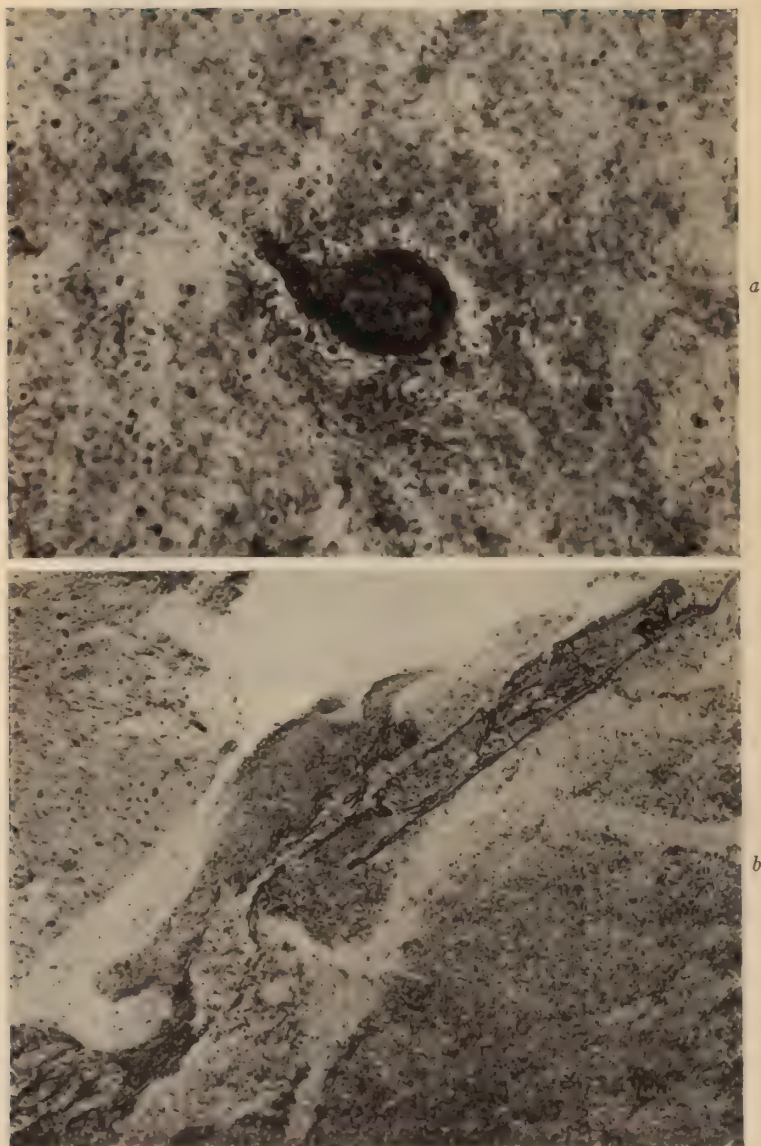


FIG. 5. (a) Small vessel floating in the hemorrhagic mass. (b) Small vessel with defect in its degenerated wall.

the hemorrhagic focus. Within the coagulum there were recognized small, exposed blood vessels with walls showing advanced degeneration, but still intact (fig. 5a). Then again, within the same coagu-

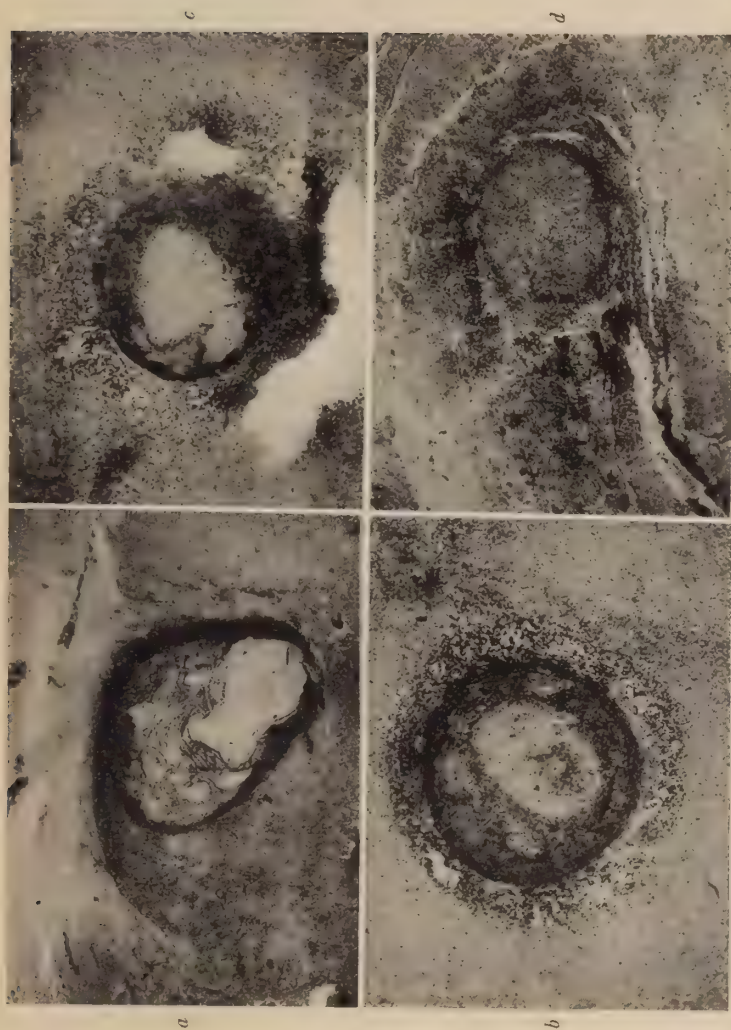


FIG. 6. A vessel at various points in its course through a hemorrhagic area: (a) thrombosed and recanalized; (b) surrounded by a zone of leucocytes and lymphocytes with its wall showing advanced degeneration; (c) the vessel is partially patent but its wall shows more advanced degeneration; (d) the vessel wall almost completely disintegrated and being washed away by the blood stream.

lum of blood, vessels were present displaying advanced disintegration of the vessel wall, which at one point had given way to extravasation (fig. 5*b*). In another quadrant of the same hemorrhagic cavity a partially thrombosed and recanalized blood vessel was found (fig. 6*a*). Its wall showed evidence of advanced hyalinization, and, at one point, extreme thinning, as though on the point of rupture. The adventitia (perivascular) was distended with extravasated blood which at one point appeared to have merged with the surrounding

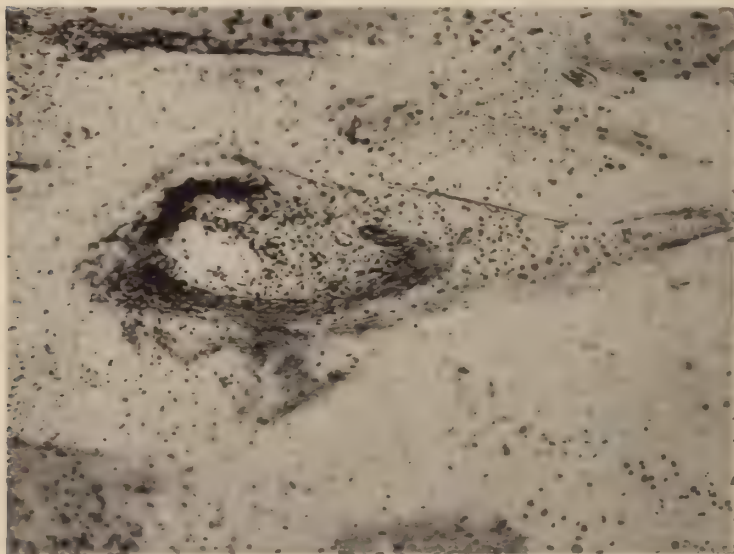


FIG. 7. An artery in a small hemorrhagic lake, showing disrupted vessel wall and ruptured adventitial coat.

hemorrhage. This vessel was followed in its course through a series of sixty consecutive sections and its alterations at various levels could be readily studied. Thus at a level twenty sections remote from the first section it was found almost completely thrombosed, its wall quite necrotic and surrounded by a zone of infiltration consisting of polymorphonuclear leucocytes and an admixture of lymphocytes and blood cells (fig. 6*b*). This infiltration, in turn, was surrounded by a coagulum of blood. At still another point the same vessel, only partially thrombosed, displayed marked disorganization of its wall

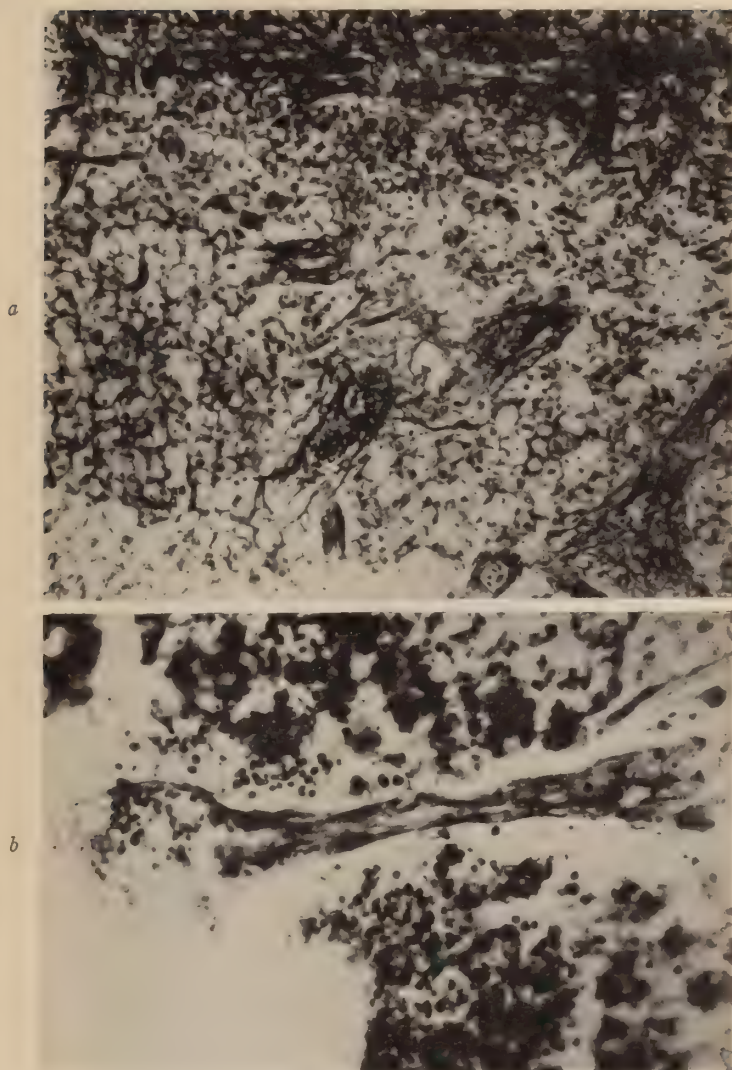


FIG. 8. (a) Lining of hemorrhagic cavity. (b) Pseudo-aneurysmal termination of a vessel projecting into the hemorrhagic cavity.

(fig. 6c). It seemed to have been the segment of the vessel at which extravasation took place through a defect in its wall. At a short distance from this level the same vessel was found to be represented by a

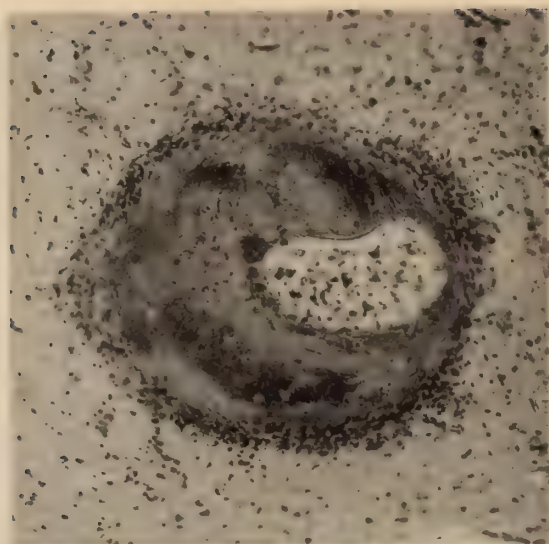
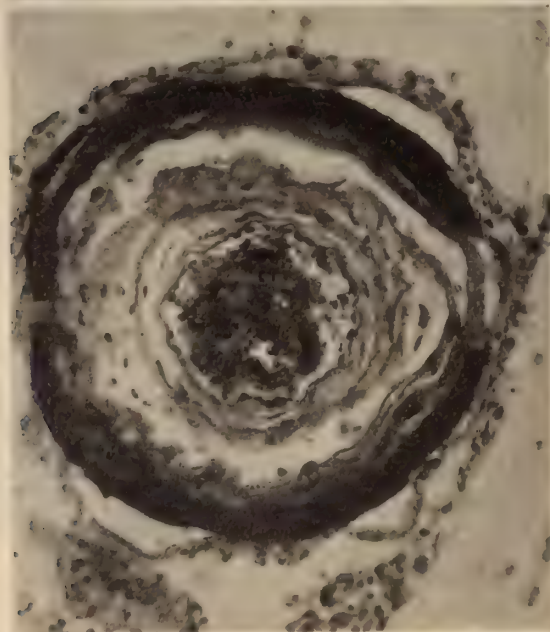
*a**b*

FIG. 9. (*a* and *b*) Arteriosclerotic vessel in the proximity of the hemorrhagic area.

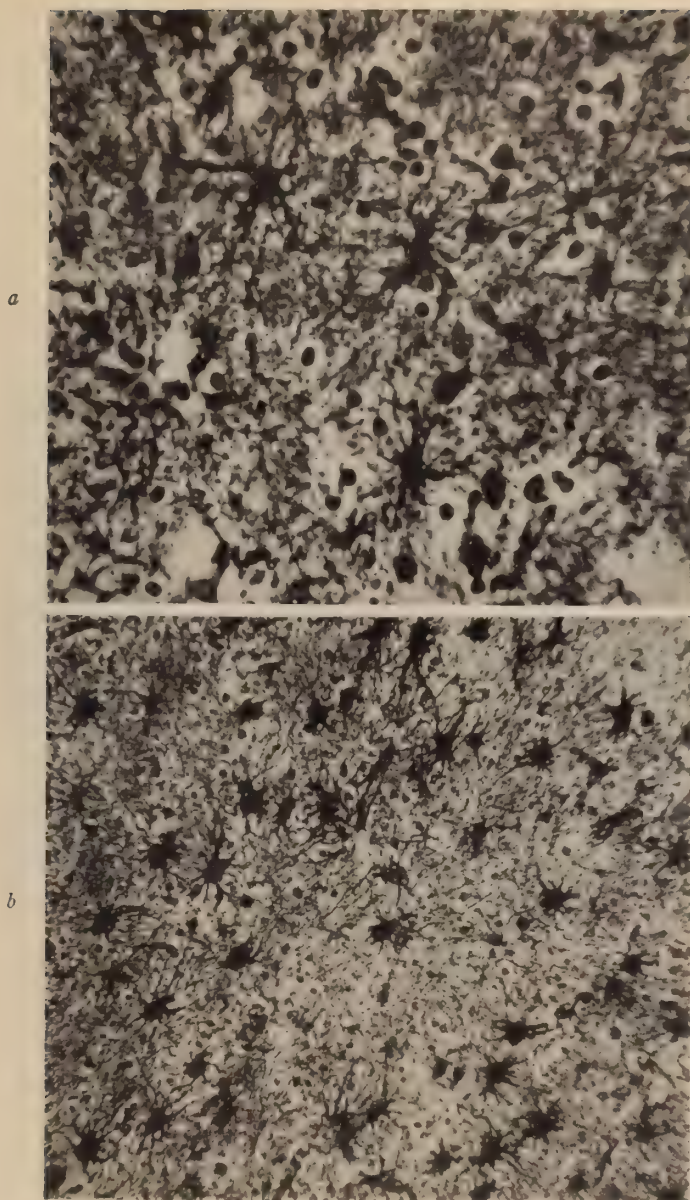


FIG. 10. (a) Glial clasmotodendrosis. (b) Astrocytic gliosis in the brain substance adjacent to the hemorrhagic zone.

mere outline of its wall (fig. 6d). The latter had undergone almost complete disintegration and its contents merged with the coagulum of blood enveloping it. Near the periphery of the hemorrhagic zone smaller hemorrhagic lakes contained vessels with clearly visible rents in their walls (fig. 7), with an adventitial space distended with extravasated blood. The perivascular space was also found torn, permitting the escape of blood into the surrounding blood lake.

The extrahemorrhagic territory. The hemorrhagic cavity was, with but few exceptions, found to be lined by remnants of softened brain

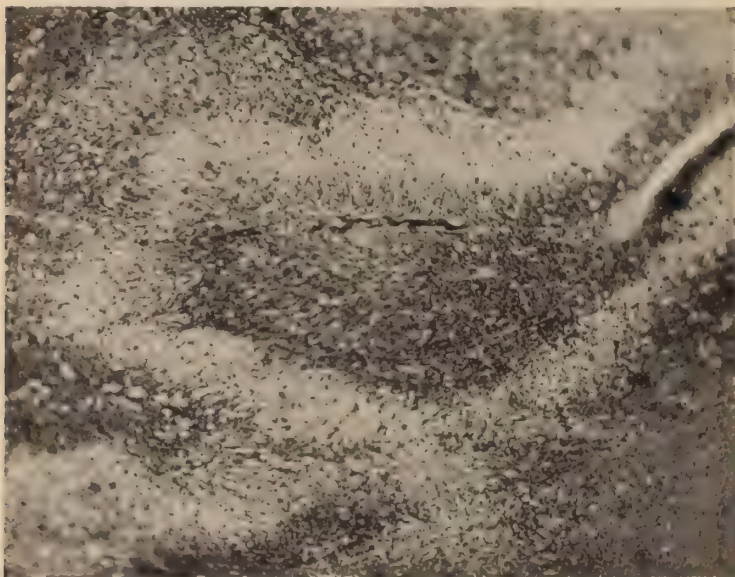


FIG. 11. Areas of rarefaction in the proximity of the hemorrhagic area

tissue. The latter consisted of many congested blood vessels embedded in a mass of compound granular cells (fig. 8a). Many of the vessels could be followed into the hemorrhagic cavity and were found to terminate in aneurysmal dilatation (fig. 8b). The latter often displayed defects through which blood apparently was escaping.

The zone of frank encephalomalacia could be followed into another zone of milder tissue disintegration. Here were many vessels displaying various stages of advancing arteriosclerosis (fig. 9), as well as many astrocytes showing degenerative alterations, such as

swelling and fragmentation of their processes (fig. 10a). Beyond this zone and at variable distances from the hemorrhagic focus, there was abundant evidence of a widespread degenerative encephalopathy,

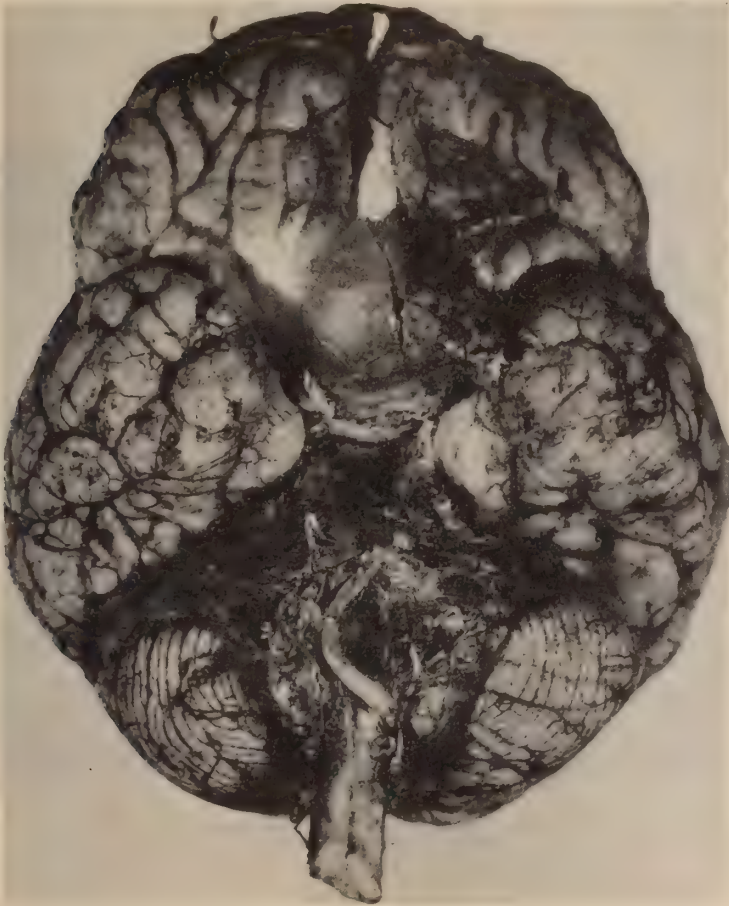


FIG. 12. Aneurysm of the Circle of Willis (left anterior cerebral branch)

secondary to the equally widespread disease of the blood vessels. It was characterized by a diffuse gliosis (fig. 10b), by areas of rarefaction (fig. 11), by foci of demyelination and small areas of encephalomalacia.

The vessels at the base of the brain. In all cases examined, the grossly visible arteries, particularly those at the base of the brain, showed advanced changes. In one case there was a large aneurysm (fig. 12) which, during the many years of its existence, caused an erosion in the overlying brain substance. The patient had four admissions to the hospital, each time arriving with the full clinical picture of subarachnoid hemorrhage. A potential cavity was thus created (fig. 13) which was finally flooded by blood through a defect in the aneurysm.

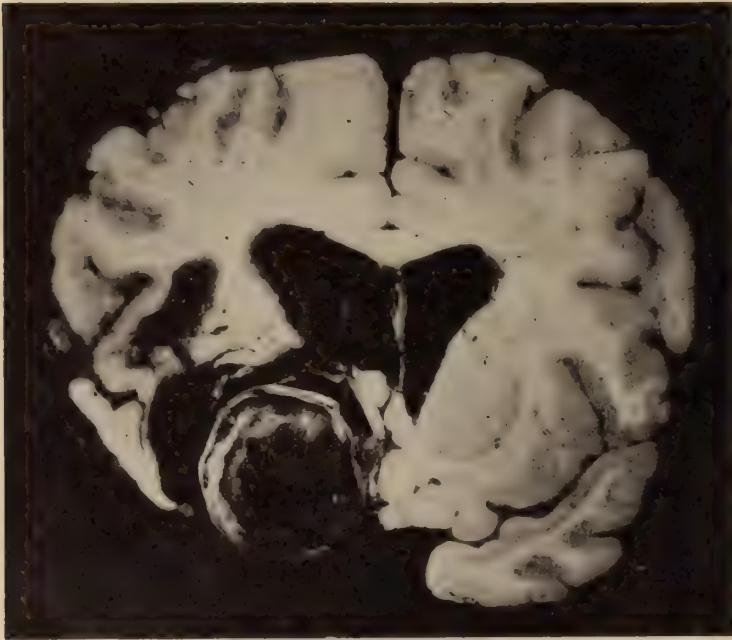


FIG. 13. Aneurysm of the left anterior cerebral artery (see fig. 12), causing disintegration and cavitation in the adjacent brain tissue.

Comment on the anatomical findings. The gross and microscopic studies of the material under investigation seem to lend support to the view, already previously expressed, that spontaneous massive cerebral hemorrhage is a terminal occurrence in a brain already affected by disease. The disease of the brain has its source in a primary process of degeneration of its blood vessels. At first the disintegration of brain tissue is minimal in quantity and very slow in advance because of the interrelationship of the vascular branches (figs. 14 and 15),

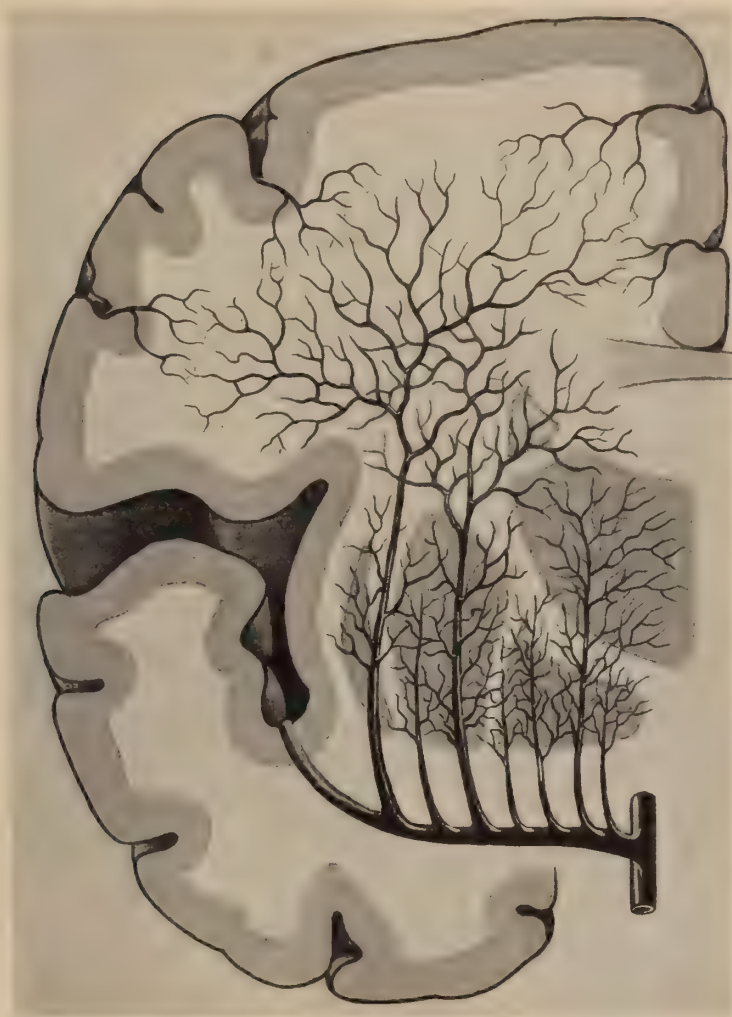


FIG. 14. Diagram illustrating the arrangement of the basal branches of the middle cerebral artery.

but as the closure of a selected vessel becomes more or less complete, the disorganization of tissue assumes larger and graver proportions (fig. 16). Thus an area of softening is formed. It is still partially,

though not adequately, nourished by branches of adjacent vessels. But with the advancing interruption of blood flow through the main nourishing channels, the area of softening enlarges and assumes the character of a potential cavity (fig. 17). In this way vessels traversing this area on the way to other parts of the brain become exposed in their course through this "cavity." These vessels, in themselves, by virtue of the general vascular disease, are not at all normal, and the proximity to poorly nourished tissue exposes them to further



FIG. 15. Drawing (after Pfeifer) illustrating the anastomotic arrangement of the basal branches shown in figure 14.

deterioration with the result that they, too, are destined to give way and rupture at one or more points. It is in this way that the cavity is flooded with blood (fig. 18).

It seems not inappropriate at this point to report some observations so as to place them on record, in view of the somewhat misleading assertions which have been made by other investigators. No true

miliary aneurysms of the type of Charcot and Bouchard were found in any of the cases herein reported. Equally erroneous is the state-



FIG. 16. Schematic drawing illustrating the probable effects of closure (by thrombosis or embolus) of a cerebral vessel. The shaded area indicates the advance of softening.

ment made by Schwartz that the hemorrhagic lesions are exclusively in the thalamo-lenticular region and found only in exceptional in-

stances in the pons. It is my experience that they may often be found in other parts of the brain, as can be noted in the accompanying



FIG. 17. Schematic drawing showing further advance in the softening process, with the production of a potential cavity.

photographs (fig. 19), although it is true that they are most frequently encountered in the thalamo-striatal zone.

SUMMARY AND CONCLUSIONS

The clinical and anatomical observations herein presented suggest that massive spontaneous cerebral hemorrhage is a terminal phase in a



FIG. 18. Schematic drawing suggesting the probable effects of the rupture of vessels traversing an area of softening.

chain of events which has its origin in a more or less diffuse disease of the cerebral blood vessels. It, in turn, is commonly associated with generalized arteriosclerosis, hypertrophy of the heart, advanced

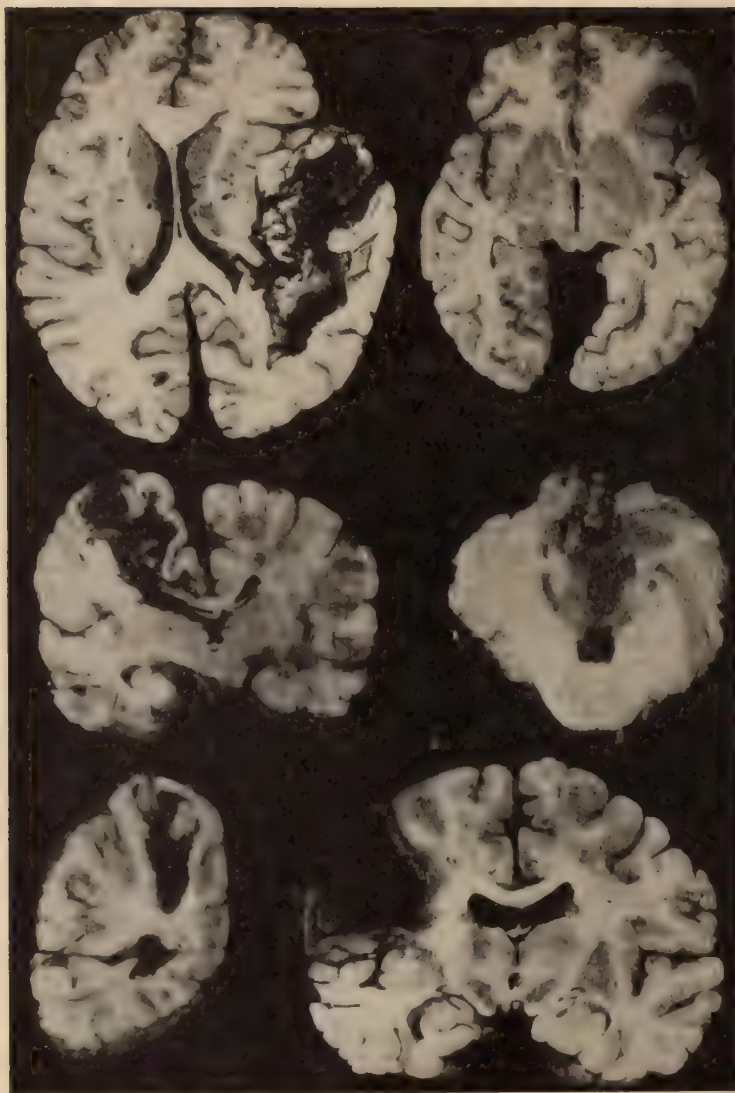


FIG. 19. Photographs of parts of several brains, displaying the variability in the localization of spontaneous massive cerebral hemorrhage.

disease changes in the kidneys, and hypertension in which both the systolic and diastolic pressures are elevated. This vascular affliction assumes a more outspoken form in some parts of the brain, resulting

in the closing of one or more of the vessels delegated to such territories. Ischemic zones with subsequent softening and circumscribed areas of lowered brain cohesion develop. The creation of such an area of softening may precede the fatal hemorrhage by a period of time extending over years, months or days, and in some instances, probably by even shorter periods of time. Such an area is commonly traversed by still patent, and hence functioning, vessels. These vessels, no longer surrounded by normal brain tissue and affected by the disturbed circulation, undergo degenerative changes. The entire process, including the necrobiosis of tissue and vessels, is not a static one. It progresses with further disintegration of the still patent, but exposed, blood vessels. At the same time as the softening process advances, the hypertension is unrelieved, if not advanced. Thus the disease of brain and vessel marches on until the time arrives when the vessels give way at some point in their course through the area of diminished brain resistance. They break and the cavity is flooded with blood. This cavity is surrounded by softened and readily yielding brain tissue. Only a narrow rim of such tissue separates it from the adjacent lateral ventricle or from the subarachnoid space. This yields to the pressure of the accumulating blood, which breaks through and floods either the ventricles or the subarachnoid space. The fatal issue is then inevitable, and occurs most rapidly when the hemorrhagic cavity ruptures into the ventricle; it is somewhat delayed when it breaks into the subarachnoid space. All this occurs without the intervention of external forces, without imposed violence or obvious sharp alterations in the physiologic state of the organism, but as the result of the gradual evolution of intrinsic disease factors, such as the insidious degeneration of blood vessels, the disintegration of brain tissue,—both conditions progressing under the influence of the pulsating impact of a hypertensive blood stream propelled by a hypertrophic heart.

DISCUSSION

The following question submitted to Dr. Globus before the Commission, together with the answer to it, is here reported verbatim.

DR. WILLIAM CHASE (Montreal, Canada): I am sorry I missed the first few minutes of Dr. Globus' paper. I would like to ask one question, that is whether or not he thinks that the small hemorrhages at the top, that is the more passive

ones, are the result of the secondary ruptures or are they extensions from the primary larger focus?

DR. JOSEPH H. GLOBUS (New York): I would say that they probably are part of the entire pathological picture, but I cannot fully dismiss the possibility that alterations in the vascular network beyond the area of the hemorrhage may not occur on the basis of vasomotor disturbances.

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PHRENIC NERVE INTERRUPTION IN PARA-ESOPHAGEAL HERNIA

REPORT OF TWO CASES

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These two cases are briefly reported to direct attention anew to the use of a simple procedure in one type of diaphragmatic hernia. Designed as a palliative measure or, in some instances, as a preliminary step to a more extensive operation, phrenic nerve interruption not only gives prompt relief, but is often of lasting benefit in cases of hernia of the stomach through the esophageal hiatus of the diaphragm.

Case 1. (S. G., Adm. 356687.) A married woman, 57 years old, was admitted to the Semi-Private Pavilion on September 5, 1933. In 1932 I had done an arthrotomy of the knee, removing several joint mice and a torn semi-lunar cartilage. This was her only serious illness except the complaint which brought her to the hospital for the second time. For six weeks following a very severe attack of right upper quadrant pain she had persistent distress and soreness in the upper abdomen. The acute attack was the third in three years, and by far the most severe. Her pain radiated to the back and she had required morphine for relief. A roentgen-ray study of the gall bladder prior to admission showed poor filling and distortion of that organ.

She was a short, very obese woman who had slight tenderness in the region of the gall bladder and nothing else of note in the physical examination. At operation on September 6, a thin-walled gall bladder containing eight stones was found adherent to the duodenum. The gall bladder and the appendix were removed. Exploration of the remainder of the abdominal contents disclosed nothing abnormal.

The postoperative course was stormy from the beginning. The patient vomited persistently in spite of lavage and a Levin tube. The vomitus remained coffee-ground in appearance. She suffered with epigastric distress and a sense of oppression in the lower chest. The pain often radiated to the shoulder. She found difficulty in breathing when lying down and remained propped up on pillows. Hiccough developed and would come on in attacks frequently during the day and night. Her stools showed melena. Her hemoglobin fell from eighty per cent on the fifth postoperative day to seventy-two per cent on the twenty-first, and sixty per cent on the thirtieth day after operation.

The clinical picture was certainly far removed from any of the usual complications following a cholecystectomy. Finally a diagnosis of hernia of the stomach through the esophageal hiatus suggested itself, and was proved by X-ray studies (Figure 1).

The question then arose as to how this condition could best be treated. Radical repair seemed out of the question so soon after a cholecystectomy, especially in a short fat individual. Interruption of the phrenic nerve was known to be used as a

preliminary procedure before radical repair, and in a few cases as a palliative operation. On October 3, the left phrenic nerve was exposed in the neck, and crushed. The operation had to be carried out with the patient in the sitting position as her respirations were too embarrassed in the prone posture. Immediately following the crushing of the nerve she exclaimed "What have you done to me, my breathing is easier and the pain in my chest has gone?" She was relieved from pain from that time, but vomiting persisted for several days. A week after this operation she went home.

In the four and a half year interval she has had two or three days on which there was mild epigastric distress, but is well-satisfied with her condition.

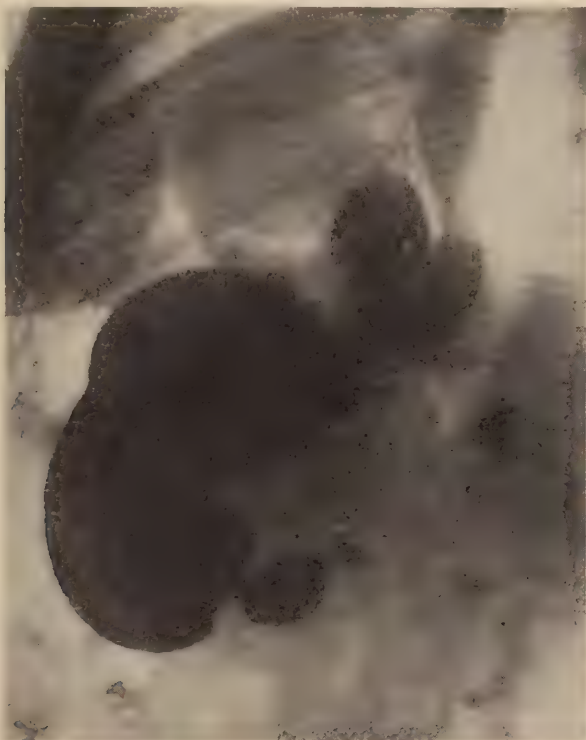


FIG. 1. Para- esophageal hernia of the stomach

Whether in the case here reported an error in diagnosis was made, I am unable to state. It is possible that the cholelithiasis was the cause of the patient's complaints, and the herniation a postoperative complication which came on acutely. In favor of this was the persistent vomiting from which she had not previously suffered. Somewhat against it was the persistent bleeding which is more likely to appear in a hernia with ulceration from long incarceration.

Case 2. (H. F. N., Adm. 414454.) A 49 year old man was admitted to the Neurological Service in September 1937 for the relief of attacks of vertigo. His illness

dated back ten years when, without warning, he suddenly became dizzy, vomited, and lost consciousness for a few minutes. Similar episodes occurred about once a year during the succeeding years. During the past four years, there was buzzing in the right ear, most noticeable during an attack of vertigo, and gradual loss of hearing on that side. For many years the patient had had indigestion, heart-burn, and eructations.

The general examination showed a blood pressure of 160 systolic and 102 diastolic and a moderate enlargement of the prostate. Rapid motion of the head produced transient dizziness. There was loss of caloric response on the right and diminution of hearing on that side. Laboratory studies threw no additional light on the condition. The spinal fluid was under normal pressure and contained a total protein of fifty-four. A diagnosis of a Menière syndrome was made and section of the right eighth nerve advised. At the operation bleeding was so troublesome that by the time the nerve was visualized the patient's condition made discontinuance of the operation advisable. He vomited repeatedly on the table and it was noted that the vomitus was bloody.

Among the various postoperative complications, vomiting of bloody fluid was prominent and epigastric distress persistent. Gastro-intestinal X-ray examinations showed a para-esophageal hernia. Five weeks after the craniotomy, the left phrenic nerve was sectioned under local anesthesia. The epigastric distress persisted for a few days, but since that time there has been complete relief which has persisted for one year since the nerve interruption. Re-examination by X-ray of the gastro-intestinal tract failed to show evidence that the para-esophageal hernia remained.

In a review of one hundred and five cases of diaphragmatic hernia which he observed, Harrington points out that seventy-six of them were through the esophageal hiatus. In all but three of them the stomach alone was the herniating viscus. In his series, the palliative operation on the phrenic nerve was carried out eight times.

Whenever intestines with or without the stomach form the herniating viscus, a closure of the opening to prevent intestinal obstruction seems imperative. When the stomach alone is in the sac, to await the result of a phrenic nerve interruption seems a justifiable procedure.

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UTERINE BIOPSY CURETTAGE—ITS VALUE IN DIAGNOSIS OF GENITAL TUBERCULOSIS

REPORT OF A CASE

SEYMOUR WIMPFHEIMER, M.D.

[From the Gynecological Service of Dr. I. C. Rubin]

Tuberculosis of the upper genital tract, the uterus and adnexae continues to be a problem in clinical diagnosis. The following case is presented because the diagnosis was established by a simple procedure—uterine biopsy curettage. By the use of a small curette sufficient endometrium was obtained for pathological examination. Dilatation of the cervical canal was unnecessary. A minimal amount of trauma was produced in obtaining the specimen.

CASE REPORT

History (M. B., Adm. 409890). The patient was 17 years old and not married when she was first admitted to the hospital on February 4, 1931. At that time she was operated on for acute appendicitis. The appendix was found to be one inch in width and four inches long, necrotic to the cecum, so that the stump had to be inverted. The postoperative course was complicated by hyperpyrexia and the development of a mass in the left lower quadrant. The mass, however, disappeared when the wound began to discharge, but an abdominal sinus persisted. Later, by means of lipiodol injections, the sinus was found to extend into the cecum. The fistula closed spontaneously after ten months.

Two years later the patient, at the age of 19, was readmitted, this time to the Gynecological Service, because of recurrent attacks of pain in the left lower quadrant. The menses were normal until the two periods before admission. These occurred four days before the expected time. There was no dysmenorrhea or leukorrhea.

On pelvic examination a globular, cystic mass, the size of a grapefruit, was felt on the left side. The uterus could not be clearly defined. The right adnexae were adherent low in the pelvis.

The patient had lost 17 pounds in the previous three months. She had resided with her father who had been treated for pulmonary tuberculosis.

X-ray examinations of her chest made at Bellevue and at this hospital showed her lungs to be negative for tuberculosis.

The diagnosis was either an adnexitis of tuberculous origin or a tubo-ovarian abscess secondary to the appendicitis.

The patient was opposed to any operative interference. She was observed in the Follow-up Clinic for a period of ten months during which time the mass decreased but continued to be the size of a tangerine.

About this time the patient was married and failed to return for further observation.

On June 10, 1937, almost six and one-half years after the first admission to the hospital, she was readmitted to the Gynecological Service with a history of an attack of left lower quadrant pain lasting about three weeks associated with a daily

afternoon chill and temperature rise to as high as 106°F. During the four days before admission there was vomiting with severe headaches. A tender nodule had developed on the inner aspect of each arm, noticed four days before admission. For the past four years the menses had been irregular, occurring at varying intervals between seven and sixty days. The periods had become scanty, lasting only three

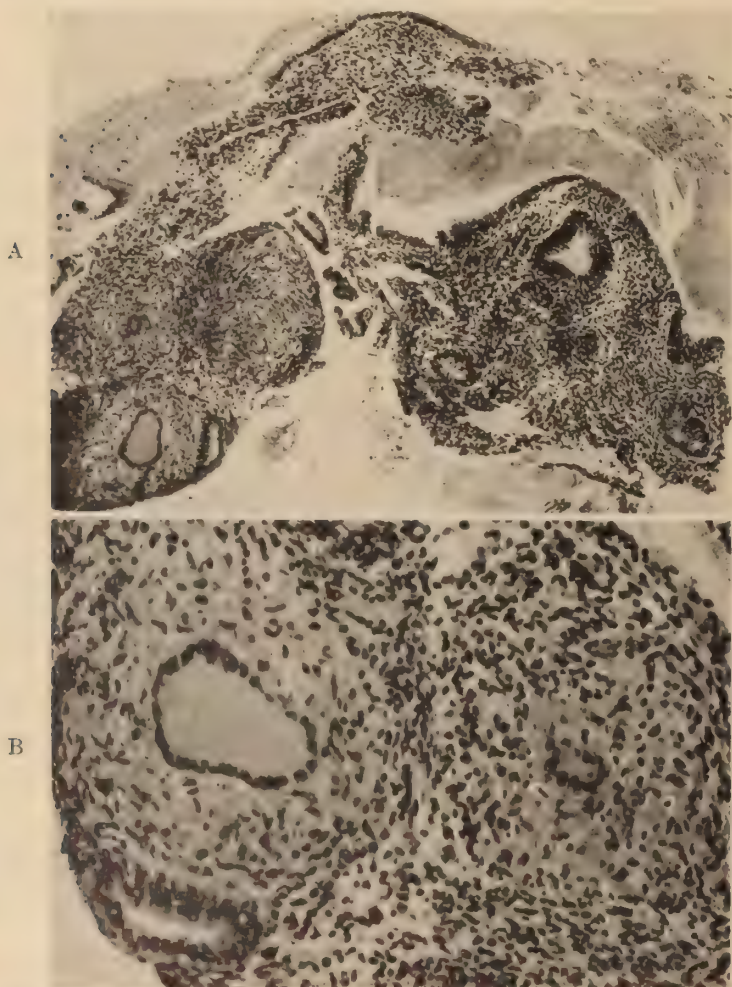


FIG. 1. A. Low power. Showing tuberculous endometritis. B. Higher power. An area in A showing a giant cell typical of tuberculosis.

days instead of the usual five days, the flow being diminished. The last menstrual period had occurred on June 5, five days before admission.

Examination. The patient was a normally developed but undernourished female about twenty-four years of age. She was pale and appeared acutely ill. The examination of the head, neck and chest were essentially negative. There was an area of tender induration on the inner aspect of each arm: the right, three centimeters in diameter; the left, one and one-half centimeters in diameter.

Abdominal examination revealed a spasm of the muscles of the left lower quad-

rant. A mass reaching to the level of the umbilicus was palpated. On pelvic examination there was a fixed, cystic mass, about ten inches in diameter, occupying the left side of the pelvis. The uterus could not be defined. The right adnexa were thickened and fixed. The introitus was nulliparous.

Temperature on admission was 104.6°F. Sedimentation time was thirty-nine minutes. There was a marked leucocytosis, white blood count being 20,000 (88 per cent polymorphonuclear leucocytes). There was a secondary anemia (hemoglobin, 60 per cent).

The differential diagnoses considered were: (1) a generalized miliary tuberculosis from the pelvic focus, (2) a septicemia from a pelvic focus of pyogenic origin.

Blood cultures were negative for both aerobic and anaerobic organisms. Two Loewenstein cultures failed to show any tubercle bacilli. A uterine biopsy curettage, suggested by Dr. I. C. Rubin, revealed a "tuberculous endometritis" (Figs. 1A and B). This procedure, performed on the ward without anesthesia, established the diagnosis of genital tuberculosis. X-ray examinations of the chest showed only a calcified area in the region of the hilum of the right lung but no evidence of recent disease. Guinea-pig inoculations of the blood and urine were reported negative for tuberculosis. An examination of the ocular fundi was normal. A biopsy of the skin nodules revealed only chronic non-specific inflammation.

In view of the positive evidence of uterine tuberculosis and because of the frequent association of adnexal and uterine tuberculosis it may be assumed that the pelvic mass was involved in the same process. There was no clinical evidence of generalized miliary tuberculosis.

Any form of surgical therapy was considered hazardous. Simple drainage of the mass was deemed inadvisable because of the possible introduction of secondary infection or the formation of a tuberculous fistula. Radical extirpation of the tuberculous process was contra-indicated because of the patient's poor general condition. Radiotherapy was therefore instituted, six exposures of 75 R being given to three anterior and three posterior pelvic fields. There was no improvement in her clinical status. The hyperpyrexia persisted for six weeks, the temperature reaching 104°F. each afternoon. She was transferred to another institution for further treatment. The patient became more emaciated, the abdomen became slightly distended but no ascites developed, the anemia increased. The fever continued, although somewhat diminished. Signs of amyloid disease became manifest. X-ray examinations of the chest continued to be negative. The urine continued to be negative for tubercle bacilli. The patient developed a tuberculous enteritis. She died four months after the onset of the last stage of her illness.

DISCUSSION

The indication for uterine biopsy curettage as a diagnostic procedure is made apparent by the high incidence of endometrial involvement in pelvic tuberculosis. The uterus, according to Jameson (1) is involved in 50 per cent of all cases of genital tuberculosis and is exceeded in frequency only by the Fallopian tubes which are affected in 85 per cent of the cases. Uterine tuberculosis is frequently associated with tuberculous salpingitis. Simmonds (2) found the uterus affected in 74 per cent of his cases of tuberculous tubes, while Menge (3) states that the association occurs in 60 per cent of the cases. Spaeth (4) gives an incidence of 55 per cent. Kelly and Noble (5) feel that most instances of tuberculous salpingitis are accompanied by endometrial tuberculosis.

The endometrium is most often involved while the myometrium is

rarely affected. Greenberg (6) in a study of 200 cases of tubal tuberculosis, found the uterus involved ninety times, an incidence of 45 per cent. He noted that the disease was localized to the endometrium in seventy-eight cases and to the myometrium in four cases while both were affected eight times. Bush (7) also recognized the prevalence of the endometrial lesion in a study of thirty-one cases of genital tuberculosis in which the uterus was affected in fifteen instances.

The importance of careful examination of curettings was emphasized by Martin (8) who found twenty-four cases of tuberculous endometritis in 1,600 routine examinations of uterine mucosa. By careful microscopic examination Cullen (9) collected forty cases of tuberculous endometritis in six years. Greenberg, in addition, reports that he performed dilatation and curettage sixteen times in his 200 cases of tuberculous salpingitis and found thirteen cases showing tuberculous mucosa, an incidence of 81.2 per cent. Bush advises routine curettage to determine whether the uterus is involved.

In view of these findings, endometrial biopsy would be indicated in cases of suspected adnexal or uterine tuberculosis. In the case presented, a small curette was employed to obtain sufficient endometrium for microscopic examination. However, the suction cannula can also be used.

If there is no disturbance in the menses, the procedure should be performed during the premenstrual phase as it has been demonstrated that the lesion first is found localized to the functional layers of the endometrium and may be cast off during the menstrual flow. One should, however, only consider positive evidence of value.

SUMMARY

1. A method is presented for the diagnosis of pelvic tuberculosis.
2. It is rapid, simple, and can be performed as an ambulatory procedure.
3. It can be repeated if clinically suspicious.
4. It should be done premenstrually, if possible.
5. Literature indicates that the endometrium is frequently involved in pelvic tuberculosis. Therefore, this approach is logical.

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PHAGEDENIC ULCER TREATED WITH ZINC PEROXIDE

NATHAN MINTZ, M.D.

[*From the Surgical Service of Dr. Ralph Colp*]

In the last decade there has come into gradually increasing prominence a type of phagedenic ulcer characterized by its unusual chronicity, invasive powers, and peculiar bacteriological phenomena, the first case of which was described by Meleney in 1926. Since then about twenty cases have been reported, each of which fulfilled the clinical and bacteriological requirements.

The disease is aptly called a "chronic undermining burrowing infectious ulcer" which respects neither sex nor age and may involve any part of the body. The portal of entry may be either an accidental or operative wound, but on occasion the organism has been known to invade the regional lymph nodes and not produce the lesion at the site of entry. The original habitat of the organism is obscure.

The bacteriological criteria are fairly specific. The responsible organism is a micro-aerophilic hemolytic streptococcus which can be best obtained by anaerobic culture and only sparsely, if at all, by aerobic methods. After artificial cultivation on meat medium, it gradually takes on aerobic qualities. The colonies are small and gray and are surrounded by a clear hemolytic zone with a diameter two or three times the size of the colony. The organism shows the usual cultural characteristics of the beta-hemolytic streptococcus, and Meleney believes that it may have been originally an ordinary aerobe which has adapted itself to an anaerobic environment. Repeated cultures taken from an ulcer that is being actively treated show a progressive reduction in the number of streptococci and a gradual loss of their hemolytic zone, the latter replaced by a greenish tinge.

The lesion is characterized by prolonged suppuration with a slow, steady advance of the undermined rolled-in ulcer margin. Sinuses are formed which tend to burrow under the skin or into deeper tissues, causing almost a liquefaction of the subcutaneous tissues. Because of this marked tendency toward burrowing, daughter ulcers may be produced by a perforation of the skin from beneath; and later the bridge of tissues separating the two ulcers breaks down, resulting in their fusion. The base of the ulcer is covered with a purulent exudate which can be easily wiped off and leaves a raw, oozing surface of indolent, unhealthy granulations.

A low grade fever is almost always present, sometimes accompanied by constitutional symptoms, and usually by a moderate amount of local

pain and tenderness. The infectious process rarely extends into muscle or bone but when it involves the latter, the outlook for a cure is almost hopeless. It rarely invades the blood stream, but several cases have been noted in which the local process actually eroded into a vessel and caused profuse hemorrhage. Due to the chronic suppuration, secondary amyloid degeneration of the kidneys, spleen, and liver may be encountered.

This condition is not to be confused with a gangrenous type of ulceration of a chronic nature caused by synergistic action of a non-hemolytic micro-aerophilic streptococcus and the staphylococcus aureus. The latter lesion is more superficial, has no undermining of skin margins and no sinus formation. There is an area of gangrene surrounded by a raised purple zone, which is in turn surrounded by an area of erythema. The organisms can usually be cultured from the lesion.

Because of the anaerobic qualities of the organism, it occurred to Meleney that the ordinary antiseptic ointments would be of no avail, and that the ideal agent must be a chemical that could give off nascent oxygen in the tissues over a period of hours or days. After some experimentation he decided on zinc peroxide as the most suitable vehicle.

Extreme care must be taken to be sure that the zinc peroxide is of the utmost purity and effectiveness, and is obtained as a finely divided white powder having the consistency of talcum. The powder is sterilized in a dry oven at a temperature of 140 degrees C. for a period of four hours, and then mixed with equal parts of sterile distilled water to obtain a suspension having the consistency of 40 per cent cream. Due to conditions apparently beyond the control of the manufacturer, some batches may be obtained in which the proportion of available nascent oxygen is greatly reduced, and these samples are practically worthless. Accordingly, Meleney devised a simple technique for the testing of the efficiency of each batch. An effective sample when placed in a test tube of water should sediment very rapidly, leaving almost a clear, supernatant fluid. Within a few hours there may be observed the production of gas bubbles in the sediment which serves as an index to the amount of nascent oxygen being generated. The details of the treatment will be considered in the following case report.

CASE REPORT

History. (F. A., Adm. 415525.) The patient was a 26 year old Jewish house-wife who was admitted to the hospital on October 18, 1937, with the following history. In June of the same year, the patient had gone to a beauty parlor to obtain a permanent wave and during that process sustained a moderately severe second degree burn on the left side of the neck. She applied a soothing lotion to the area, but several days later noted the presence of a painful swelling there, which increased progressively in size and severity. Her physician was called who told her that an abscess had formed which would require an incision. This was accordingly done; a small amount of pus was obtained, but inadequate drainage established because the abscess continued to discharge. Two weeks later another incision was required which

likewise failed to have the desired effect, and the pain, tenderness, and discharge continued unabated. In the meantime, the patient noted that the infection had begun to spread with simultaneous loss of skin over the involved area. The patient tried various forms of lotions and ointments, none of which had the slightest effect on the progress of the lesion or the amount of discharge. A third operation was performed several weeks later but again without any measure of success. To her knowledge a culture of the lesion had never been taken. The patient was rapidly becoming discouraged and despondent, not only because of the pain and tenderness that she experienced but also because of the exposed location of the involved area, so that she could not bear to be seen among her friends. Matters continued in this state until she entered this hospital on October 18, 1937.

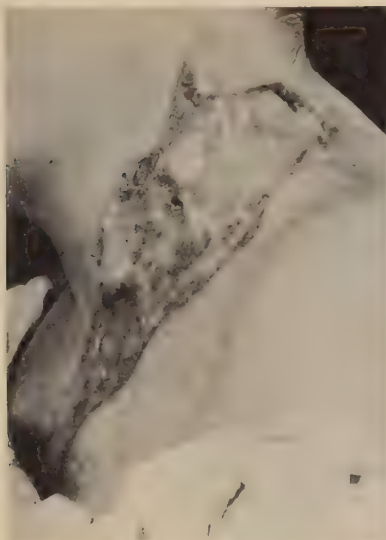


FIG. 1

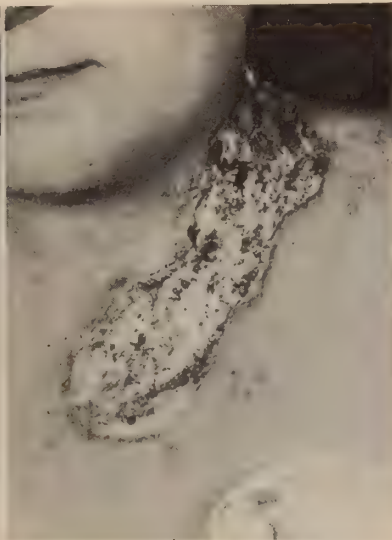


FIG. 2

FIG. 1. Appearance of the lesion after the patient had been on the ward for one week.

FIG. 2. Appearance of the lesion after zinc peroxide treatment had been instituted. Note that the ulcer has become smaller in size and that the margins are not undermined.

Examination. The patient was a rather obese, white female in no acute distress, but in a marked state of mental depression. On the left side of her neck, extending approximately from the level of the upper third of the anterior border of the trapezius muscle downwards and forwards almost to the level of the sterno-clavicular junction there was a roughly oval, ulcerated area, measuring about seven by three inches. The margins were irregular, almost serpiginous, thickened and rolled in with a considerable amount of undermining. The base of the ulcer was somewhat depressed, extending into the subcutaneous tissue, and covered by a layer of pale pink, unhealthy, indolent granulation tissue on top of which was a moderate amount of grayish-yellow, purulent exudate. Any attempt to wipe away the discharge caused considerable pain and oozing. The surrounding tissue was slightly indurated and erythematous. At no point was there any evidence of the slightest healing, and one received the impression of a slowly progressive but relentless infection

which extended in all directions by a process almost of liquefaction of skin and subcutaneous tissue. The remainder of the examination was essentially negative.

Laboratory Findings. The hemoglobin was 82 per cent. The white cell count was 10,450 per cu. mm. with a differential of 50 per cent segmented forms, 22 per cent non-segmented forms, 16 per cent lymphocytes, and 2 per cent monocytes. The urine was negative. The temperature never rose above 100°F. A biopsy of the skin margin showed non-specific ulceration of the skin with acute diffuse inflammation. A second biopsy taken about a week later showed a chronic ulcer with foreign body reaction.

Course. The diagnosis of a chronic undermining ulcer due to the micro-aerophilic hemolytic streptococcus was made on admission, confirmed bacteriologically, and treatment with zinc peroxide begun immediately. Dr. Frank L. Meleney of the Presbyterian Hospital kindly consented to see the patient and suggested several

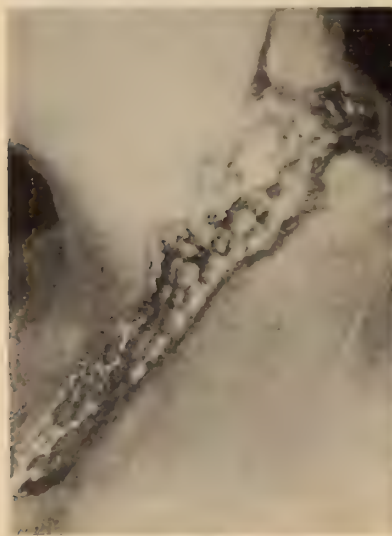


FIG. 3



FIG. 4

FIG. 3. Appearance of the lesion after pinch graft

FIG. 4. Appearance one year after discharge, the patient to receive radiotherapy

modifications in the treatment which proved extremely helpful. We were also indebted to him for a gift of a tested active preparation of the zinc peroxide. A definite regime was outlined and followed religiously. Each morning the ulcer was carefully cleansed with warm saline in order to wash away the exudate, and a fresh mixture of the zinc peroxide prepared. The entire area was then flooded with the suspension and a rubber catheter inserted under the overhanging edges to insure contact of every part of the ulcer with the mixture. The area was then covered with a layer of fine mesh gauze soaked in the suspension, care being taken to insert it under the margin. The part was then covered with vaseline gauze to prevent evaporation. As an adjuvant to zinc peroxide therapy, sulfanilamide was given in divided doses of 60 grains a day, but was stopped after one week because of the appearance of minor toxic symptoms.

Within a few days definite improvement was noticed. The spontaneous pain had stopped, the granulations appeared healthier, and advance of the ulcer margins

had been halted. However, the undermining persisted, and on November 6, under gas-oxygen anesthesia, the overhanging walls were excised by means of the actual cautery, so that the ulcer margin was now beveled off almost level with the base.

Cultures taken at frequent intervals showed a diminution in the number of colonies of hemolytic streptococci, and on November 8, it was reported that the colonies were no longer hemolytic but had acquired a greenish tinge. On November 12, there were no longer any streptococci present.

The healing continued now without interruption. The base was clean and healthy, the advance of the lesion checked, the undermining stopped, the discharge gone, and new skin was beginning to grow in from the margin. On November 17, under avertin and gas-oxygen anesthesia, about 20 to 25 pinch grafts were applied to the neck, both thighs being used as donor sites. Not more than $\frac{1}{16}$ of an inch was allowed between each graft; the area was covered with a single layer of coarse mesh gauze, and the skin margin sealed with collodion. On top of this were now placed several layers of fine mesh gauze soaked in saline and covered with vaseline gauze to prevent evaporation. Twenty-four hours later the fine mesh gauze was carefully removed, the area flooded with zinc peroxide, and again covered with fine mesh and vaseline gauze. Forty-eight hours later, the entire dressing was removed and it was seen that fully 95 per cent of the grafts had taken. The daily applications of zinc peroxide were continued until the patient was discharged on November 24, 1937. When the patient was seen in the Follow-up Clinic on January 19, 1938, it was noted, "skin graft on area completely healed; no suggestion of residual infection. To return one year later for cosmetic improvement."

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PURULENT MENINGITIS PRODUCED BY THE MINUTE HEMOLYTIC STREPTOCOCCUS (LONG & BLISS) AND B. COLI

ALEXANDER THOMAS, M.D.

[From the Laboratories of The Mount Sinai Hospital, New York City]

In 1934 Long and Bliss (1) reported the isolation of a new form of hemolytic streptococcus which they called the *minute hemolytic streptococcus*. The distinguishing characteristic of this organism is the very small size of the colony, often microscopic at first, with a relatively increased size of the surrounding zone of hemolysis on a blood plate. The organisms themselves occur in pairs, short chains, and masses and are one-half to one-third the size of the ordinary hemolytic streptococcus. Long and Bliss isolated over 200 strains of this organism from human throats, especially in patients with rheumatic fever and nephritis. Two strains were obtained in pure culture from the pus of acutely inflamed paranasal sinuses and one strain from the pus of a chest wall abscess. On the basis of their cultural characteristics, sugar reactions, and reactions with sodium hippurate and methylene blue milk, Long and Bliss suggested that these organisms may represent a new species of streptococcus. They could find no previous descriptions of these organisms in the literature (2).

The following case of otitic meningitis with sepsis is presented because it is the first case in which this minute hemolytic streptococcus has been isolated from the cerebrospinal fluid or blood stream. The case is also of bacteriological interest because of the presence of a *B. coli* infection of the mastoid and meninges in addition to the streptococcal infection.

CASE REPORT

History (Adm. 408701). The patient, a 4-year old male child, was admitted to the hospital on May 17, 1937 with a three months' history of purulent discharge from the left ear. The past history was negative. Three months before admission, following an upper respiratory infection, there was the onset of a profuse, thin, purulent discharge from the left ear. The discharge then became thick and creamy. Three days before admission the mother noted feverishness in the child. The patient complained of pain in the left ear on the same day. Swelling and tenderness behind the left ear were noted on the day of admission.

Examination. The patient appeared acutely ill. The right ear was normal. The left ear showed a foul, purulent discharge from an anterior perforation. Left post-auricular edema and tenderness was present. The lungs showed a patch of diminished breath sounds with crackling râles over the right upper lobe. Neurological examination showed a left peripheral facial paresis, bilateral Babinski signs, stiff neck, and a slightly positive Brudzinski sign. There were no Kernig signs.

Laboratory Data. Hemoglobin, 82 per cent; white blood cells, 21, 200 (88 per cent polymorphonuclear leucocytes). Spinal fluid on admission showed 40 cells with 60 per cent polymorphonuclear neutrophils. On smear, a number of Gram-positive cocci, some in small chains, were seen.

Course. On the night of admission a complete simple mastoidectomy with exploration of the petrous pyramid was performed. The mastoid was completely broken down. The dura was covered by a greenish-yellow exudate. The patient did not respond to the operation or subsequent treatment with transfusions, pron-tosil, and *B. coli* phage and died eleven days after admission.

Post mortem examination showed purulent meningitis secondary to a left middle ear and mastoid infection.

Bacteriology. The first two spinal fluids showed only small Gram-positive diplococci and cocci in small chains on smear. On culture, including pour plates, only *B. coli* grew out. Mice were injected, but again only *B. coli* was recovered from the peritoneum and heart's blood. Culture of the mastoid pus gave *B. coli*, though smear showed also Gram-positive cocci. The third spinal fluid showed Gram-negative bacilli and Gram-positive cocci on smear. The culture showed *B. coli* again and, in addition, one small round smooth colony on the ascitic agar plate. Transplant of this colony to blood agar showed in twenty-four hours a wide zone of hemolysis along the line of the streak, but no colonies visible grossly. The next day the zone of hemolysis was wider with very small translucent colonies composed of small Gram-positive cocci.

The blood culture taken on the second day after admission grew out the same streptococcus in all flasks. Post mortem culture of the meningeal pus showed *B. coli* and this same minute hemolytic streptococcus. Blood pour plates of this streptococcus showed pin-point colonies with wide zones of surrounding hemolysis. Many of the colonies did not become visible until after forty-eight to seventy-two hours of growth.

The organism was studied for its fibrinolytic power (3) and serological type according to the method of Lancefield (4), as is done routinely with all hemolytic streptococci in the bacteriology laboratory of The Mount Sinai Hospital. A broth culture of the organism was incubated with oxalated human blood plasma to which calcium chloride had been added. Partial lysis of the plasma clot occurred, indicating a moderate fibrinolytic power. It is interesting to note that almost all strains of pathogenic human hemolytic streptococci are fibrinolytic.

A saline extract of a broth culture of the organism was then incubated with specific rabbit antisera for each of the Lancefield types from A. to G. Precipitation occurred with type F. This is the type into which Long's strains (2) fell, although Lancefield considered its pathogenicity for humans still uncertain (4). It is of interest that of the hundreds of strains of hemolytic streptococcus isolated from human infections studied in the department of bacteriology of this hospital, this organism was the first one encountered which fell into type F.

COMMENT

The isolation of the minute streptococcus hemolyticus offered great difficulty in this case because of its small size and the presence of *B. coli*. It is of interest that even though the organism was definitely pathogenic for man in this case it fell into Group F of Lancefield.

B. coli meningitis itself, although it is usually considered the most frequent type of meningitis in the new-born (5), is already a rare type at the age of 4 years. Josephine Neal (6), in a series of 1,535 cases of menin-

gitis, found only five cases due to the colon bacillus, of which three were under one year of age. In a review of the literature in 1926 Neal (7) found forty-two cases of *B. coli* meningitis reported.

The incidence of mixed infections in cases of meningitis is also very small. In the same series of 1,535 cases Neal found six cases of mixed infections. The majority of cases of mixed infections reported in the literature have been due to either the meningococcus or tubercle bacillus with another organism. The only case of mixed meningitis seen previously by the chief bacteriologist of this hospital (8), in a large experience, was a case due to the pneumococcus type III and the influenza bacillus. This patient recovered.

Thus, this case presented several unusual bacteriological features, the most important of which was the isolation for the first time of this minute hemolytic streptococcus from the spinal fluid and blood stream.

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SYMPATHETIC PLEURAL EFFUSION IN LUNG ABSCESS

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[From the Department of Radiology and the Chest Group]

Sympathetic pleural effusion is an uncommon accompaniment of putrid lung abscess. Iselin (1) published a comprehensive paper on the subject in 1933. The following case of acute putrid lung abscess with sympathetic effusion is presented to illustrate the difficulty in diagnosis and in localization of the abscess when the complicating sympathetic effusion is present.

CASE REPORT

History (Adm. 416329). The patient, a 59 year old white male, was readmitted November 6, 1937 having been treated for *tabes dorsalis* two months previously at this hospital. Four days before admission, the patient developed weakness, nausea, and pain in the back of the right chest. His temperature at this time was 101°F. During the following three days the temperature curve was septic in type, the temperature finally rising to 106°F. at the time of admission. On admission he developed a non-productive cough.

Examination. The patient appeared extremely toxic and was somewhat disoriented. He had the typical physical signs of fluid in the right chest. In spite of the temperature of 106°F. and the apparent disease in the right chest, his respirations were only 22 per minute.

Only after inducing the patient to cough vigorously was the examining physician able to detect a foul odor to the breath. The patient then expectorated a small globule of purulent material containing red blood. It was therefore considered that the cause of the pleural fluid was a gangrenous lung abscess.

Roentgen examination. The postero-anterior view showed an effusion in the right chest. Above this was an area of rarefaction which could have represented an abscess. The antero-posterior view (Fig. 1) showed the abscess cavity better delineated and demonstrated a fluid level. The effusion was seen to dip into the short interlobar fissure and to extend along the axillary border and over the apex of the lung. An antero-posterior, lateral recumbent view was also made with the patient lying on his left side (Fig. 2). This view proves the presence of the fluid level by its shift with a change of the patient's position. The right lateral erect view (Fig. 3) localized the abscess to the apex of the right lower lobe at the level of the sixth rib posteriorly, which, incidentally, was the region over which the patient felt his pain.

Diagnostic aspiration of the pleural fluid showed it to be clear and, later, cultures proved it to be sterile, thus establishing the pleural fluid as a sympathetic effusion.

Operation. The abscess was approached postero-laterally by resecting the sixth rib. Thickened pleura was encountered within which a small pool of foul pus was found directly over the site of the lung abscess. This was drained. The abscess was a projecting gangrenous, hemispherical mass, two inches in diameter, which had not perforated but, in the words of the operator, appeared to be on the verge

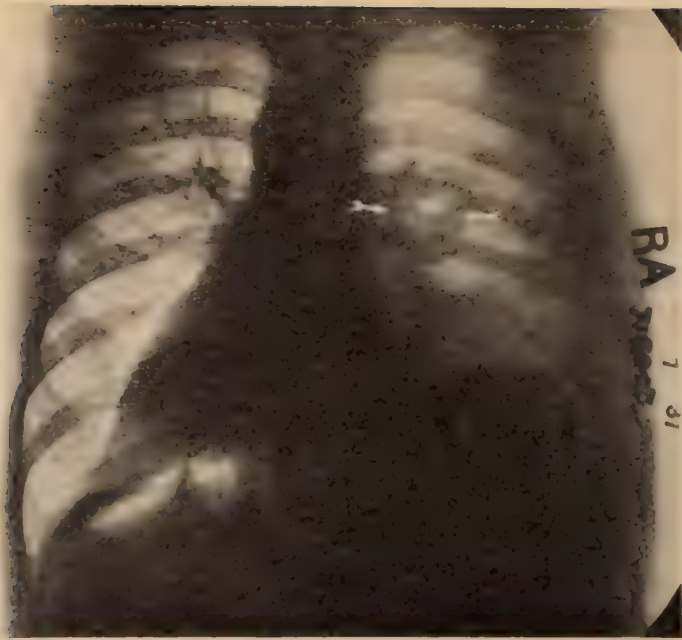


FIG. 1. Antero-posterior view. An effusion is seen in the right chest extending up along the axillary border, dipping into the short fissure and over the apex of the lung. An abscess cavity is noted at the level of the sixth interspace posteriorly.



FIG. 2. Lateral recumbent view. A fluid level within the cavity is seen to be horizontal, evidently having shifted with change in the position of the patient.

of perforation. Small lakes of clear fluid were discovered in the trabeculations of fibrin adjacent to the abscess site. The abscess was then treated by resection of its roof and partial excision of the gangrenous lung tissue adhering to its floor. A small bronchial fistula was noted. The usual closure with packing was performed.



FIG. 3. Right lateral view. The abscess cavity is seen to be situated in the apex of the right lower lobe. A fluid level is again noted within the cavity.

The patient was discharged one month after operation with a healing incisional sinus and complete resorption of the pleural exudate.

The etiology of the abscess was undetermined. It was suggested that the abscess might have been contracted during a hyperpyrexia treatment given for the tabes dorsalis.

COMMENT

This case illustrates that an acute putrid lung abscess may not only produce a sympathetic pleural effusion but that it may be of such extent as to mask the physical findings and alter the clinical picture of putrid lung abscess. The effusion, furthermore, tends to make the roentgen diagnosis of lung abscess more difficult by obscuring the lesion. Confusing shadows caused by pleural loculations also tend to render roentgen interpretations difficult.

In those cases where the abscess is completely obscured by a massive effusion or for any concomitant cause, it is suggested that aspiration of the fluid may expose the underlying lesion to view roentgenologically.

It is interesting to note in this case that at operation a small pool of foul pus was found directly over the non-perforated abscess, and that about this were small lakes of clear fluid caught in the fibrin trabeculations. This is significant in that it probably represented the first stage of a pyothorax that could conceivably have developed *without perforation* of the abscess. A similar observation was made by Wessler and Jaches (2).

Accurate localization of a putrid lung abscess, although always desirable, is particularly essential in the presence of a sympathetic pleural effusion, so as to avoid operative contamination with its resultant pyopneumothorax.

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Walter L. Horn

March 1, 1891–December 29, 1938

The flag over the entrance to the hospital was again at half-mast on December 29, 1938, bearing the sad message that another of our colleagues had departed. Walter Horn, one so young and endeared to so many, was taken from our midst by the unkind hand of destiny.

A surgeon of high attainments, he spared no effort to gain greater skill and worked tirelessly to keep abreast with scientific progress in his chosen field. He ignored warnings and refused to submit to restrictions in carrying out the tasks of his busy days, although he was fully aware that his health demanded constant vigilance and long periods of rest. Instead, he would often, after a day crowded with exacting work, devote many a late hour to study. It was thus that he was able to contribute his share to creative scientific work, which included the extensive clinical and anatomical study on "The Inherent Healing Properties of Brain Abscess," published in the Archives of Otolaryngology. It was of such quality as to merit editorial mention in the Journal of the American Medical Association. He continued to labor almost to his last, giving his ebbing time and declining strength to another, equally important and nearly completed work on acoustic tumors.

To his patients he brought with his surgical excellence unbounded kindness, good cheer, and sincere devotion. Ever ready to give his best when called upon to care for the sick, he took little heed of the perils threatening his own health.

To his colleagues he was generous almost to a fault and unflinching in his loyalty.

Deep is the sorrow of all who knew Walter Horn, and long will his memory be cherished by all who witnessed his kindness to the afflicted, his devotion to his friends, and his scrupulous performance of his duties during eighteen years of service at The Mount Sinai Hospital.

JOSEPH H. GLOBUS.

ABSTRACTS

AUTHORS' ABSTRACTS OF PAPERS PUBLISHED ELSEWHERE BY MEMBERS OF THE MOUNT SINAI HOSPITAL STAFF

Members of the hospital staff and the out-patient department of The Mount Sinai Hospital are invited to submit for publication in this column brief abstracts of their articles appearing in other journals.

Complications of Successful Thoracoplasties. A. H. AUFSES. Am. Rev. Tuber. 35: 464, April, 1937.

The criterion of a successful thoracoplasty is a negative sputum and no demonstrable cavity. The type of thoracoplasty which is at present being performed, occasionally leads to complications which do not manifest themselves until some period of time has elapsed after operation.

(1) Scoliosis occurring after operation, may cause marked deformity of the spinal column. (2) Fixation of the scapula following partial upper thoracoplasty may be due to fixation of the angle of the scapula under the next intact rib. Fixation may also follow an infection of the subscapular area. (3) Cardiac hypertrophy may occur after any form of pulmonary fibrosis. Following thoracoplasty, a considerable part of the pulmonary tissue is reduced to a hard fibrotic mass, thereby setting the stage for the later development of myocardial hypertrophy. (4) Bronchiectasis is one of the results of the healing of pulmonary tuberculosis by fibrosis. It may be present before operation is performed and may be an invaliding symptom afterwards. Two case histories are presented of patients who were cured of their tuberculosis by thoracoplasty, but who remained invalids due to the persistence of a severe bronchial dilatation. Six pictures and x-ray films illustrate the conditions discussed.

Phrenic Nerve Operations in the Treatment of Pulmonary Tuberculosis, a review. A. H. AUFSES. Medicine 16: 139, May 1937.

A complete review is made of the entire subject of phrenic nerve operations in the treatment of pulmonary tuberculosis, with a bibliography of 593 references. The contents deal with (1) history (2) anatomy and physiology (3) effect on respiration, cough and expectoration, pathology, intrapleural pressure, venous blood pressure, blood supply (4) mode of action (5) technique of operation (6) tests of diaphragmatic paralysis (7) aids to paralysis (8) temporary paralysis (9) return of function (10) indications (11) contra-indications (12) bilateral paralysis (13) complications (14) effect upon gastro-intestinal tract (15) effect upon heart (16) results.

The opinions of various authors on controversial matters are stated without prejudice. Seventeen thousand five hundred and seventy phrenicectomies, as reported by 142 authors, have been collected. The results of seventy-eight authors who reported as "cured," "healed," or "arrested," are given for 10,567 operations. Of these, 435 were performed as independent procedures with 734 (23.3%) "cures". Seven thousand and three operations were reported by sixty-four authors using the terms "improved," "working," etc. Of these, 5,648 were performed as independent operations with 2,837 (50%) improved.

The Relation of the Blood Group Specific Substance A to the Type Specific Carbohydrate of Pneumococcus Type I. H. SOBOTKA, E. WITEBSKY, E. NETER, AND ELEANOR S. SCHWARZ. *J. Infect. Dis.* 60: 257, May-June 1937.

The specific carbohydrate fraction from cultures of *Pneumococcus* type I grown on a medium free of blood group A substance, was tested for its reactivity towards blood group A antiserum. It displayed definite although moderate activity, while an analogous fraction obtained from non-inoculated medium was almost inactive. Specific soluble carbohydrate prepared from washed *Pneumococcus* type I also proved active towards A antiserum.

It will be difficult to decide between the possible explanations of this cross-reaction, before the chemical nature of the blood group substance is further elucidated.

Newer Methods of Treating Hemorrhage Due to Ulcer. B. B. CROHN. *Am. J. Digest. Dis. & Nutrition* 4: 256, June 1937.

This editorial deals with the question of feeding an ulcer during the active hemorrhage, an idea sponsored and suggested by Meulengracht of Copenhagen, Denmark. He believes in giving the patient "something to eat" in large quantities and freely throughout the hemorrhage. He reports a total mortality of 1.2 per cent in a series of cases. The contention of Meulengracht, that those who starve ulcer cases have a higher mortality, is criticised and the figures are shown to emanate from a small series of cases without modern methods of handling, or to be based upon material restricted only to the extreme type of gross hemorrhage from ulcer.

The author feels that such a radical change from the one extreme of starving hemorrhage cases to the other extreme of feeding in large quantities is a dangerous experiment. His own experience with the starving of hemorrhage cases is satisfactory, not much greater than that of Meulengracht, and a safer procedure.

The possible dire consequences of a seemingly rash procedure should call for deliberation before proceeding without more experience and caution.

Hepatic Excretion in the Dog Following Oral Administration of Various Bile Acids.

H. DOUBILET. *Proc. Soc. Exper. Biol. & Med.* 36: 687, June 1937.

A common bile duct fistula, which drained all the hepatic bile sterily into a rubber bag, was performed in three female dogs. Cholic and desoxycholic and glycocholic and dehydrocholic acids, as well as pure ox bile salts and the natural bile acids of canine gall bladder bile, were fed in daily amounts of four to eight grams.

The results indicated that, from the point of view of the largest excretion of bile acids in most concentrated form, the natural bile acids of the dog were the most efficient. Under the conditions of these experiments, pure ox bile salts and glycocholic acid were found to be more efficient than the unconjugated cholic and desoxycholic acids. The natural bile acids (cholic and desoxycholic acids and their conjugated forms) were more effective than dehydrocholic acid.

A Combined Operation for Complete Hysterectomy. S. H. GEIST. *Am. J. Obst. & Gynec.* 33: 1081, June 1937.

An operation is described to facilitate the complete removal of the uterus and to reduce to a minimum the disadvantages of the present procedures for that purpose.

In the usual procedure the difficulties encountered usually are the result of the fixation of the cervix when the complete abdominal operation is done, and the presence of large tumors, adhesions or unsuspected conditions when the vaginal operation is done. The new technique suggested is as follows:

The routine is as for vaginal hysterectomy. A circular incision is made circumscribing the cervix and leaving a cuff of vaginal mucosa. This is dissected free and sutured in front of the cervix, thus covering that organ to prevent contamination of

the abdomen if infection is present. The bladder is elevated, the anterior peritoneal fold opened. The posterior peritoneal fold is then opened. The uterosacral ligament and the parametrium up to the uterine vessels and then the uterine vessels themselves are ligated and cut. This completes the vaginal procedure, except for fixing the parametrium and sacrouterine stump into the posterior vaginal edge. The vaginal mucosa is partly closed. An iodoform pack is inserted into the vagina. The patient is now placed in the Trendelenburg position and prepared for laparotomy in the routine fashion. On opening the abdomen such conditions as adhesions and large tumors can be readily taken care of. The infundibulopelvic ligaments as well as the round ligaments are tied and cut. The uterus can now be lifted out of the abdomen. The vaginal gauze is removed. Two narrow strips of iodoform gauze are passed through the vagina, the abdominal ends being placed in each parametrial extraperitoneal space. The abdomen is then closed in the usual way.

Biologic Assay of Estrogenic Factors in Pregnancy Urine. M. A. GOLDBERGER. Am. J. Obst. & Gynec. 33: 1093, June 1937.

The biologic assay in this study shows that the total estrins excreted in normal pregnancy is low up to the twenty-ninth week and highest between the twenty-ninth and thirty-sixth weeks. It again drops to a low level in the last four weeks of pregnancy. The free estrin excretion found in this investigation was greatest between the thirty-second and fortieth weeks.

The percentage of free estrins varies from 2 per cent to 22 per cent and shows no definite relationship to the period of pregnancy. Before drawing definite conclusions a large series of cases should be investigated.

Uterotubal Insufflation in the Macacus Rhesus. A. H. MORSE AND I. C. RUBIN. Am. J. Obst. & Gynec. 33: 1087, June 1937.

A method of assaying pharmacologic and hormonal effects by the determination of their action in the living monkey was worked out in the macacus rhesus. The physical impediment to the investigation was found to be an anatomical structure, the colliculus cervicis peculiar to the monkeys. By incising the cervix wall laterally the obstacle was easily overcome, thus permitting the introduction of a uterine cannula which, when attached to an insufflation apparatus with kymograph, enabled us to record tubal and uterine contractions before and after treatment with oxytocic, antispasmodic and other pharmacologic substances commonly employed in clinical medicine, including the more recent hormonal extracts. The report was based on preliminary work.

Rôle of Arteries in Peripheral Resistance of Hypertension. M. PRINZMETAL AND E. T. OPPENHEIMER. Proc. Soc. Exper. Biol. & Med. 36: 675, June 1937.

By means of observation of systolic pressure in the brachial and digital arteries of ninety patients, it was shown that the fall of pressure from large to small arteries (brachial-digital pressure gradient) is substantially the same in cases of chronic hypertension and in subjects with normal or with low blood pressures. This suggests that the increased resistance occurs in vessels smaller than the digital artery, not in the arteries themselves.

On the other hand, in one case of arterial spasm, and in four cases of obstructive vascular disease, there was a marked increase in the brachial-digital pressure gradient, indicating that obstruction of the arteries, whether due to spasm or to organic changes, causes an increased gradient from large to small arteries.

It seems, therefore, that in chronic hypertension the increased resistance occurs, not in the large arteries, but in vessels smaller than the digital artery.

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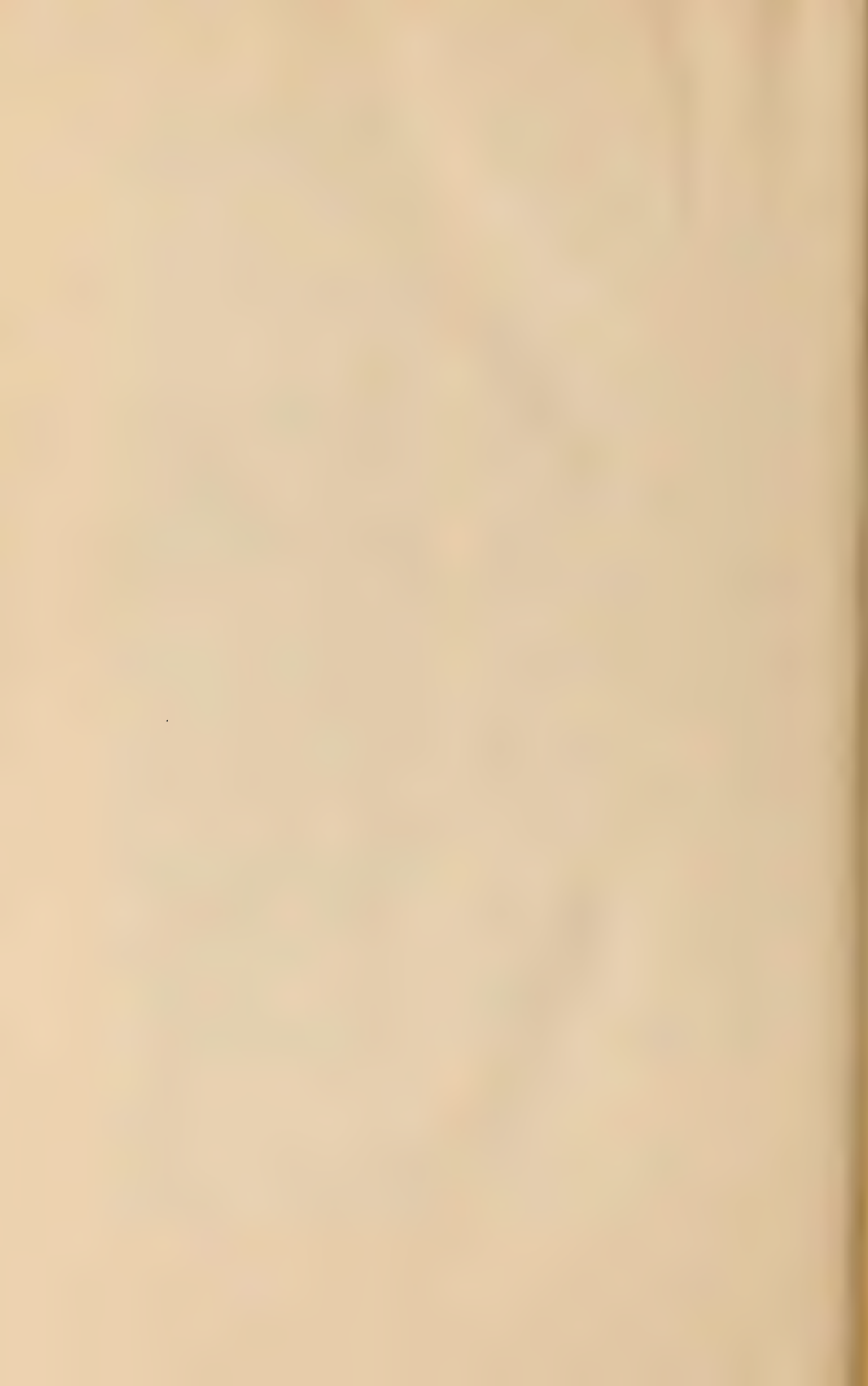
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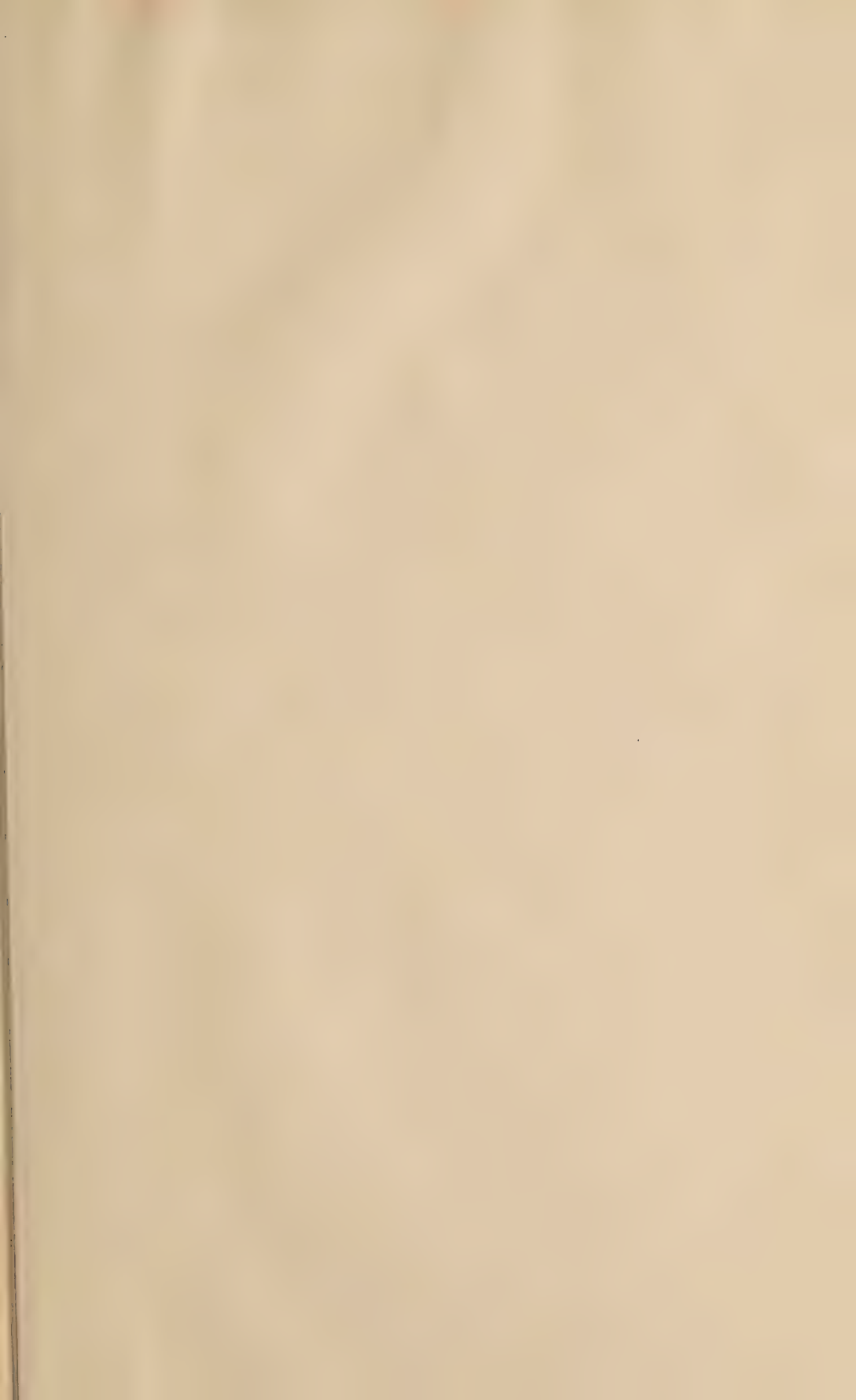
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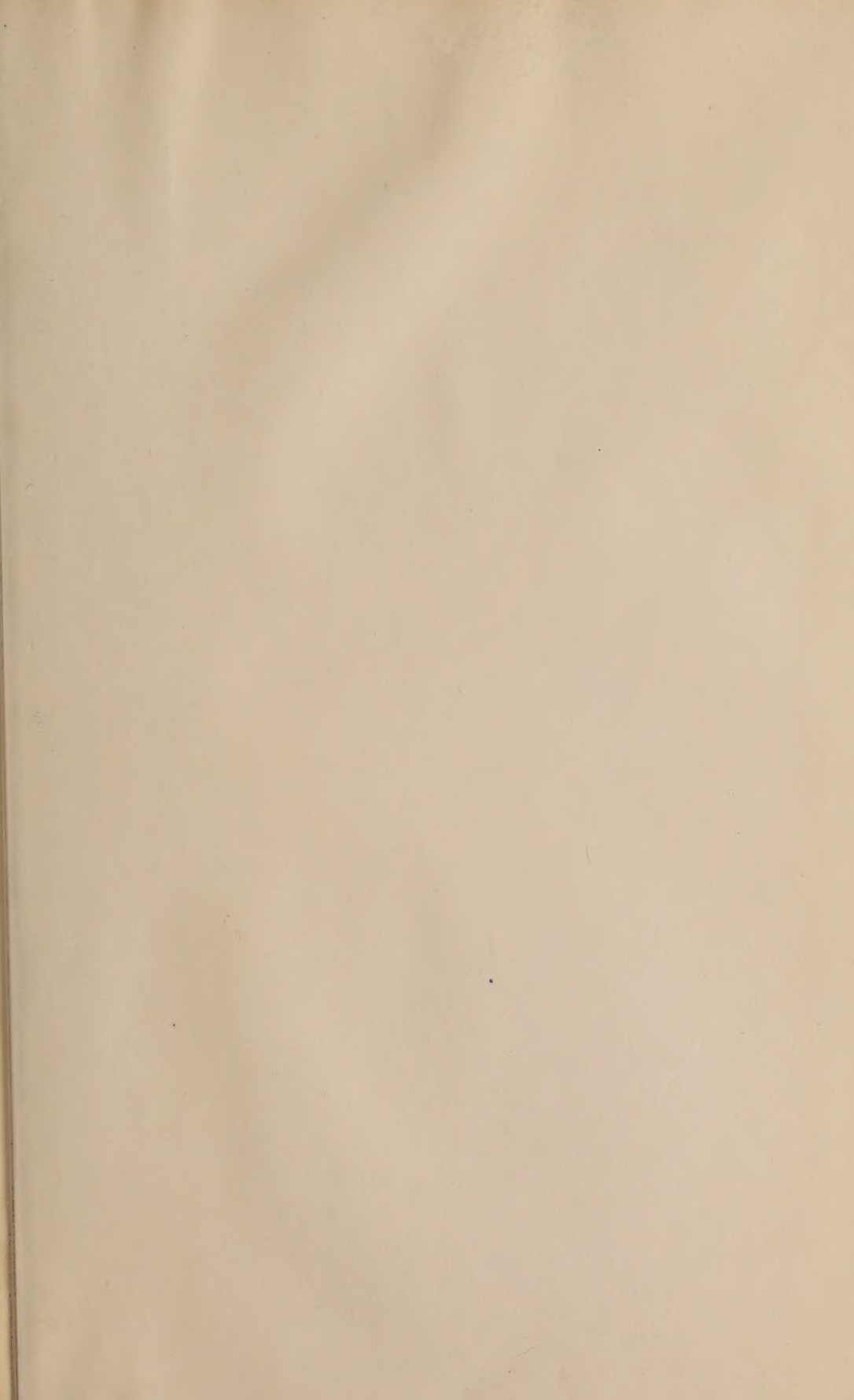
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